1355

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                    STN Columbus

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=> file medline embase scisearch biosis patoswo

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=> s fas(w)ligand or fas(w)substrate

          2798 FAS(W) LIGAND OR FAS(W) SUBSTRATE

    s (inhibit? or reduc? or antagon?)

  1 FILES SEARCHED...
  2 FILES SEARCHED...
  4 FILES SEARCHED...
L2    5150812 (INHIBIT? OR REDUC? OR ANTAGON?)

=> s monoclonal(w)antibod?

  3 FILES SEARCHED...
L3    413230 MONOCLONAL(W) ANTIBOD?

=> s fas

L4    13464 FAS

=> s (l1 or l4)(10a)l2(10a)l3

L5       62 (L1 OR L4)(10A) L2(10A) L3

=> dup rem

ENTER L# LIST OR (END):l5

L6       18 DUP REM L5 (44 DUPLICATES REMOVED)

    l6 1-18 ibib ab


L6  ANSWER 1 OF 18  PATOSWO  COPYRIGHT  1998 WILA
    WOA1 PCT-PUBLICATION
ABEN  A novel humanized immunoglobulin reacting specifically with a Fas
      ligand and active fragments thereof are provided and a region on a
      Fas ligand which is important in inhibiting apoptosis induced by
      cells with Fas expression on the basis of the Fas-Fas ligand
      interaction is clarified. The novel humanized immunoglobulin and
      active fragments thereof are prepared by the recombinant DNA
      techniques from hybridomas which produce a ***monoclonal***
      ***antibody*** reacting specifically with a ***Fas***
      ***ligand*** . This immunoglobulin can ***inhibit***
      physiological reactions between a ***Fas*** ***ligand***
      and ***Fas*** , typified by apoptosis. By specifying the region
      participating in the induction of apoptosis on a Fas ligand, there
      have been constructed recombinant proteins and peptides which
      react specially with the amino acids contained in this region to
      thereby inhibit apoptosis and are thus applicable to novel
      remedies, clinical diagnostic drugs, etc.

L6  ANSWER 2 OF 18  MEDLINE                    DUPLICATE 1
ACCESSION NUMBER:  1998148050    MEDLINE
DOCUMENT NUMBER:  98148050
TITLE:      Caspase-dependent ceramide production in Fas- and HLA
            class I-mediated peripheral T cell apoptosis.
AUTHOR:     Genestier L; Prigent A F; Paillot R; Quemeneur L;
            Durand I; Banchereau J; Revillard J P;
            Bonnefoy-Berard N
CORPORATE SOURCE:  Laboratory of Immunology, INSERM U80 UCBL, Hopital E.
            Herriot, 69437 Lyon, France.
SOURCE:     JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Feb 27) 273
            (9) 5060-6.
            Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY:  United States
            Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:   English
FILE SEGMENT:  Priority Journals; Cancer Journals
ENTRY MONTH:  199805
ENTRY WEEK:  19980504
AB  We recently demonstrated that the engagement of HLA class I alpha1
    domain induced Fas-independent apoptosis in human T and B
    lymphocytes. We analyzed the signaling pathway involved in HLA class
    I-mediated apoptosis in comparison with Fas (APO-1, CD95)-dependent
    apoptosis. The mouse mAb90 or the rat YTH862 monoclonal antibodies
    which bind the human HLA class I alpha1 domain induced the
    production of ceramide which was blocked by addition of the
    phosphatidylcholine-dependent phospholipase C inhibitor, D609.
    Furthermore, HLA class I-mediated apoptosis involved at least two
    different caspases, an interleukin-1 converting enzyme-like protease
    and another protease inhibited by the CPP32-like protease inhibitor
    Ac-DEVD-CHO. Despite similarity between Fas and HLA class I
    signaling pathways, we failed to demonstrate any physical
    association between these two molecules. We also report that the
    pan-caspase inhibitory peptide zVAD-fmk, but not Ac-DEVD-CHO and
    Ac-YVAD-CHO, inhibited decrease of mitochondrial transmembrane
    potential and generation of ceramide induced by anti-HLA class I and
    anti- ***Fas*** ***monoclonal*** ***antibodies*** ,
    whereas all three peptides efficiently ***inhibited***
    apoptosis. Altogether these results suggest that signaling through
    ***Fas*** and HLA class I involve caspase(s), targeted by
    zVAD-fmk, which act upstream of ceramide generation and
    mitochondrial events, whereas interleukin-1 converting enzyme-like
    and CPP32-like proteases act downstream of the mitochondria.

L6  ANSWER 3 OF 18  MEDLINE                    DUPLICATE 2
ACCESSION NUMBER:  97368334    MEDLINE
DOCUMENT NUMBER:  97368334
TITLE:      Thymineless death in colon carcinoma cells is
            mediated via fas signaling.
AUTHOR:     Houghton J A; Harwood F G; Tillman D M
CORPORATE SOURCE:  Department of Molecular Pharmacology, St. Jude
            Children's Research Hospital, 332 North Lauderdale,
            Memphis, TN 38105, USA.. janet.houghton@stjude.org
CONTRACT NUMBER:  R37 CA 32613 (NCI)
            CA 21765 (NCI)
SOURCE:     PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES
OF
            THE UNITED STATES OF AMERICA, (1997 Jul 22) 94 (15)
            8144-9.
            Journal code: PV3. ISSN: 0027-8424.
PUB. COUNTRY:  United States
            Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:   English
FILE SEGMENT:  Priority Journals; Cancer Journals
ENTRY MONTH:  199710
AB  Fas is expressed constitutively in colonic epithelial cells and is
    also expressed in colon carcinomas and in cultured colon carcinoma
    cell lines. However, the potential role of Fas signaling in
    mediating apoptosis in cells of this type remains unknown. We have
    developed human colon carcinoma cell models deficient in thymidylate
    synthase that demonstrate acute (TS- cells) or delayed (Thy4 cells)
    apoptosis following DNA damage induced by thymineless stress.
    Complete protection of cells from acute apoptosis and prolongation
    of delayed apoptosis was obtained following exposure to the NOK-1
    ***monoclonal*** ***antibody*** ( ***inhibitory*** to
    ***Fas*** signaling) during the period of dThd deprivation. These
    results suggested that apoptosis induced by thymineless stress was
    regulated by autocrine signaling via Fas-FasL interactions. Fas
    expression was high in both TS- and Thy4 cells. However, FasL,
    undetectable in synchronous cultures, was up-regulated in TS- cells
    at 48 hr, when cells were undergoing acute apoptosis, and in Thy4
    cells at 96 hr, correlating with the delayed onset of thymineless
    death. FasL expression also correlated with acute apoptosis induced
    in parental GC3/cl cells, commencing at 48 hr, following thymidylate
    synthase ***inhibition*** by 5-fluorouracil/leucovorin exposure.
    ***Fas*** -mediated apoptosis induced by the cytotoxic anti-
    ***Fas*** ***monoclonal*** ***antibody*** CH-11 was
    ***inhibited*** following adenoviral delivery of a Bcl-2 cDNA, and
    Bcl-2 also protected cells from acute apoptosis induced by dThd
    deprivation. Taken together, these data demonstrate a functional Fas
    system in these cultured colon carcinoma cell models, and they
    demonstrate that Fas-FasL interactions can link DNA damage induced
    by thymineless stress to the apoptotic machinery of colon carcinoma
    cells.

L6  ANSWER 4 OF 18  MEDLINE                    DUPLICATE 3
ACCESSION NUMBER:  1998013099    MEDLINE
DOCUMENT NUMBER:  98013099
TITLE:      Gamma interferon induces Fas-dependent apoptosis of
            Peyer's patch T cells in mice following peroral
            infection with Toxoplasma gondii.
AUTHOR:     Liesenfeld O; Kosek J C; Suzuki Y
CORPORATE SOURCE:  Department of Immunology and Infectious Diseases,
            Research Institute, Palo Alto Medical Foundation,
            California 94301, USA.
CONTRACT NUMBER:  AI04717 (NIAID)
            AI30230 (NIAID)
            AI35956 (NIAID)
SOURCE:     INFECTION AND IMMUNITY, (1997 Nov) 65 (11) 4682-9.
            Journal code: GO7. ISSN: 0019-9567.
PUB. COUNTRY:  United States
            Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:   English
FILE SEGMENT:  Priority Journals; Cancer Journals
ENTRY MONTH:  199801
ENTRY WEEK:  19980104
AB  Since we previously observed a remarkable decrease in the numbers of
    T cells in the Peyer's patches of the small intestines in C57BL/6
    mice following peroral infection with Toxoplasma gondii, we
    performed studies to examine the mechanism(s) whereby this decrease
    in numbers of the T cells occurs. We found that apoptotic cell death
    of CD4+ and CD8+ alphabeta T cells occurred in Peyer's patches
    following infection. Upregulation of Fas expression was observed in
    these T cells. C57BL/6-background mutant mice which lack functional
    Fas antigen did not develop apoptosis in their Peyer's patches
    following infection. Treatment of infected C57BL/6 mice with
    anti-gamma interferon (IFN-gamma) ***monoclonal***
    ***antibodies*** prevented the upregulation of ***Fas*** on
    their Peyer's patch T cells and ***inhibited*** the occurrence
    of apoptosis of these T cells. These results indicate that IFN-gamma
    induces Fas-dependent apoptosis in CD4+ and CD8+ alphabeta T cells
    in Peyer's patches in C57BL/6 mice following peroral infection with
    T. gondii.

L6  ANSWER 5 OF 18  MEDLINE                    DUPLICATE 4
ACCESSION NUMBER:  97413603    MEDLINE
DOCUMENT NUMBER:  97413603
TITLE:      Drug-induced apoptosis is associated with enhanced
            Fas (Apo-1/CD95) ligand expression but occurs
            independently of Fas (Apo-1/CD95) signaling in human
            T-acute lymphatic leukemia cells.
AUTHOR:     Villunger A; Egle A; Kos M; Hartmann B L; Geley S;
            Kofler R; Greil R
CORPORATE SOURCE:  Department of Internal Medicine, University of
            Innsbruck, Austria.
SOURCE:     CANCER RESEARCH, (1997 Aug 15) 57 (16) 3331-4.
            Journal code: CNF. ISSN: 0008-5472.
PUB. COUNTRY:  United States
            Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:   English
FILE SEGMENT:  Priority Journals; Cancer Journals
ENTRY MONTH:  199711
ENTRY WEEK:  19971102
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AB Induction of apoptosis is considered to be the underlying mechanism that accounts for the efficiency of chemotherapeutic drugs. It has recently been proposed that induction of Fas ligand (FasL) expression with subsequent autocrine and/or paracrine induction of cell death through binding to the Fas (Apo-1/CD95) membrane accounts for chemotherapy-associated apoptosis. In the present study, we analyzed the significance of FasL expression in the mediation of drug-induced apoptosis in the T-acute lymphatic leukemia model CEM. In particular, we examined the potential of the tumor drugs fludarabine, doxorubicin, and cisplatin to induce FasL expression. We also raised the question of whether apoptosis induced by these drugs occurs through the Fas pathway and hence can be blocked by the cowpox virus protein CrmA, a specific inhibitor of this pathway. All tumor drugs examined led to an increase in FasL protein. However, overexpression of CrmA had no effect on drug-induced apoptosis. Moreover, neither incubation with ***inhibitory*** ***monoclonal*** ***antibodies*** against ***Fas*** that completely prevented ***Fas*** -induced apoptosis in these cells nor pretreatment with a ***monoclonal*** ***antibody*** to FasL affected drug-induced cell death. Our observations suggest a Fas/FasL-independent mechanism for drug-induced apoptosis and exclude the involvement of caspase 1 and caspase 8 in this process [redacted] T-acute lymphatic leukemia cells.

L6 ANSWER 6 OF 18 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1998000988 MEDLINE
DOCUMENT NUMBER: 98000988
TITLE: An Fc gamma receptor I (CD64)-negative subpopulation of human peripheral blood monocytes is resistant to killing by antigen-activated CD4-positive cytotoxic T cells.
AUTHOR: Grage-Griebenow E; Baran J; Loppnow H; Los M; Ernst M; Flad H D; Pryjma J
CORPORATE SOURCE: Forschungszentrum Borstel, Department of Immunology and Cell Biology, Germany.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1997 Sep) 27 (9) 2358-65.
Journal code: EN5. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199801
ENTRY WEEK: 19980104
AB It has been demonstrated that in monocyte/T cell co-cultures activated with recall antigens, cytotoxic T cells were generated which are able to reduce the number of antigen-presenting monocytes. In previous studies we could show that a minor subset of monocytes, the Fc gamma receptor I-negative (CD64-) monocytes, exhibits significantly higher antigen-presenting capacity than the main [redacted]opulation of monocytes (> 90%) which are Fc gamma receptor [redacted]-positive (CD64+). Therefore, we addressed the question whether they are also differentially susceptible to T cell-mediated killing. In the present study we demonstrate that the CD64- monocyte subset is more resistant to killing by antigen-activated T cells than CD64+ monocytes, as indicated by a higher viability and recovery of CD64- monocytes. This mechanism involves CD95 (Fas) antigen, since monocyte death in co-cultures with antigen-activated T cells could be partially ***reduced*** by blocking anti- ***Fas*** ***monoclonal*** ***antibodies*** (mAb). In agreement with this finding, although CD95 antigen was expressed on CD64+ and CD64- monocytes at comparable levels, killing of CD64- monocytes by activating anti-Fas mAb was lower than of CD64+ monocytes.

L6 ANSWER 7 OF 18 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.DUPLICATE 6
ACCESSION NUMBER: 1998096148 EMBASE
TITLE: The Fas signaling pathway is functional in colon carcinoma cells and induces apoptosis.
AUTHOR: Houghton J.A.; Harwood F.G.; Gibson A.A.; Tillman D.M.
CORPORATE SOURCE: J.A. Houghton, Department of Molecular Pharmacology, St. Jude Children's Res. Hospital, 332 North Lauderdale, Memphis, TN 38105, United States
SOURCE: Clinical Cancer Research, (1997) 3/12 I (2205-2209).
Refs: 19
ISSN: 1078-0432 CODEN: CCREF4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Fas is expressed in colonic epithelial cells and is also expressed in colon carcinomas, although its functional significance in the regulation of apoptosis in cells outside of the immune system remains unknown. In this study, we determined the role of Fas signaling on cellular growth of cultured colon carcinoma cells and demonstrated apoptosis induced by a cytotoxic anti- Fas monoclonal antibody (CH-11) in cells of the GC3/c1 lineage (CG3/c1, TS-, Thy4) but not in HCT116 or CaCo2 cells. Growth inhibition was detected at concentrations of CH-11 as low as 1 ng/ml, and clonogenic survival studies yielded IC50 values of 3-26 ng/ml. Cytotoxicity was ***inhibited*** by ZB4, a ***monoclonal*** ***antibody*** ***inhibitory*** to ***Fas*** signaling. In addition, the survival factor Bcl-2, which has demonstrated inconsistent protective effects against Fas signaling in other systems, was inhibitory to Fas-induced apoptosis in colon carcinoma cells after adenoviral transduction. Fas was expressed at the highest levels in TS- and Thy4 cells, which were the most sensitive cell lines to Fas-induced apoptosis. FAP-1, a protein tyrosine phosphatase that interacts with the cytosolic negative regulatory domain of Fas, was expressed in each cell line but did not correlate with sensitivity to Fas-mediated apoptosis. These data have therefore identified a functional Fas pathway in colon carcinoma cells when Fas is expressed at high level. Hence, the role of Fas signaling in the regulation of apoptosis in colon carcinoma cells and its role influecing the response to treatment with chemotherapeutic agents should be further explored.

L6 ANSWER 8 OF 18 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 97280693 MEDLINE
DOCUMENT NUMBER: 97280693
TITLE: Fas-mediated apoptosis in human prostatic carcinoma cell lines.
AUTHOR: Rokhlin O W; Bishop G A; Hostager B S; Waldschmidt T J; Sidorenko S P; Pavloff N; Kiefer M C; Umansky S R; Glover R A; Cohen M B
CORPORATE SOURCE: Department of Pathology, University of Iowa, Iowa City 52242, USA.
CONTRACT NUMBER: AI28847 (NIAID)
DK25295 (NIDDK)
T32AI07260 (NIAID)
+
SOURCE: CANCER RESEARCH, (1997 May 1) 57 (9) 1758-68.
Journal code: CNF. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199707
ENTRY WEEK: 19970704
AB Of six prostatic carcinoma cell lines examined (ALVA31, DU145, JCA1, LNCaP, ND1, and PC3) by flow cytometric analysis, all were found to be positive for Fas antigen. Furthermore, of the prostate tissue specimens studied (six cases), all revealed Fas expression in benign and malignant epithelial cells. The agonistic anti-Fas monoclonal antibody (IPO-4) induced apoptosis in only two of six cell lines investigated, PC3 and ALVA31. PCR analysis indicated that all cell lines expressed normal transmembrane and death domains of Fas antigen. Using Western blot analysis, we found abundant expression of p53 in the cytoplasm of two Fas-resistant cell lines, DU145 and ND1, and did not find p53 in two Fas-sensitive cell lines, PC3 and ALVA31. Western blot and PCR analysis did not show consistent differences between cell lines examined in the expression of Bcl-2, Bcl-X(L), Bcl-X(S), and Bak. In contrast, Bax protein was not detected in two Fas-resistant cell lines, DU145 and ND1. We also showed that three Fas-resistant cell lines, DU145, ND1, and JCA1, expressed CD40, whereas the two Fas-sensitive cell lines, PC3 and ALVA31, were CD40 negative. Fas-sensitive cell lines were transfected with the cDNA encoding CD40, and the CD40-positive transfectant became more resistant to growth ***inhibition*** mediated by treatment with TNF-alpha and anti- ***Fas*** ***monoclonal*** ***antibody*** . Treatment with cycloheximide converted the phenotype of resistant cell lines from Fas resistant to Fas sensitive. Moreover, anti-Fas treatment of both resistant and sensitive cell lines induced rapid tyrosine phosphorylation or dephosphorylation of multiple proteins. These results suggest that the apoptotic machinery involved in DNA fragmentation is already in place in Fas-resistant cell lines, and thus, Fas-mediated apoptosis could be a target for therapeutic intervention.

L6 ANSWER 9 OF 18 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 97272088 MEDLINE
DOCUMENT NUMBER: 97272088
TITLE: Differential induction of apoptosis by Fas-Fas ligand interactions in human monocytes and macrophages.
AUTHOR: Kiener P A; Davis P M; Starling G C; Mehlin C; Klebanoff S J; Ledbetter J A; Liles W C
CORPORATE SOURCE: Immunological Diseases, Bristol-Myers Squibb Pharmaceutical Research Institute, Seattle, Washington 98121, USA.
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1997 Apr 21) 185 (8) 1511-6.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199707
ENTRY WEEK: 19970703
AB Human monocytes undergo spontaneous apoptosis upon culture in vitro; removal of serum from the media dramatically increases the rate of this process. Monocyte apoptosis can be significantly abrogated by the addition of growth factors or proinflammatory mediators. We have evaluated the role of the endogenous Fas-Fas ligand (FasL) interaction in the induction of this spontaneous apoptosis and found that a ***Fas*** -immunoglobulin (Ig) fusion protein, an ***antagonistic*** anti- ***Fas*** ***monoclonal*** ***antibody*** and a rabbit anti-FasL antibody all greatly ***reduced*** the onset of apoptosis. The results indicate that spontaneous death of monocytes is mediated via an autocrine or paracrine pathway. Treatment of the cells with growth factors or cytokines that prevented spontaneous apoptosis had no major effects on the expression of Fas or FasL. Additionally, monocyte-derived macrophages were found to express both Fas and FasL but did not undergo spontaneous apoptosis and were not sensitive to stimulation by an agonistic anti-Fas IgM. These results indicate that protective mechanisms in these cells exist at a site downstream of the receptor-ligand interaction.

L6 ANSWER 10 OF 18 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 97477420 MEDLINE
DOCUMENT NUMBER: 97477420
TITLE: Interleukin-1 beta converting enzyme-like protease involvement in Fas-induced and activation-induced peripheral blood T cell apoptosis in HIV infection. TNF-related apoptosis-inducing ligand can mediate activation-induced T cell death in HIV infection.
AUTHOR: Katsikis P D; Garcia-Ojeda M E; Torres-Roca J F; Tijoe I M; Smith C A; Herzenberg L A; Herzenberg L A
CORPORATE SOURCE: Department of Genetics, Stanford University School of Medicine, California 94305, USA.. katsikis@auhs.edu
CONTRACT NUMBER: AI-07290 (NIAID)
CA 42509 (NCI)
LM 04836 (NLM)
+
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1997 Oct 20) 186 (8) 1365-72.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199801
ENTRY WEEK: 19980104

AB Apoptosis of peripheral blood T cells has been suggested to play an important role in the pathogenesis of human immunodeficiency virus (HIV) infection. Spontaneous, Fas (CD95)-induced and activation-induced T cell apoptosis have all been described in peripheral blood mononuclear cell cultures of HIV-infected individuals. We have previously shown that activation-induced T cell apoptosis is Fas independent in peripheral blood T cells from HIV+ individuals. In this study, we extend and confirm these observations by using an inhibitor of interleukin-1 beta converting enzyme (ICE) homologues. We show that z-VAD-fmk, a tripeptide inhibitor of ICE homologues, can inhibit Fas-induced apoptosis of peripheral blood CD4(+) and CD8+ T cells from asymptomatic HIV+ individuals. z-VAD-fmk also inhibited activation (anti-CD3)- induced CD4+ and CD8+ T cell apoptosis (AICD) in some but not all asymptomatic HIV+ individuals. Apoptosis was measured by multiparameter flow cytometry. The z-VAD-fmk inhibitor also enhanced survival of T cells in anti-Fas or anti-CD3 antibody-treated cultures and inhibited DNA fragmentation. AICD that could be ***inhibited*** by z-VAD-fmk was ***Fas*** independent and could be ***inhibited*** with a blocking ***monoclonal*** ***antibody*** to tumor necrosis factor-related apoptosis-inducing ligand (TRAIL), a recently described member of the TNF/nerve growth factor ligand family. The above findings show that Fas-induced T cell apoptosis is ICE dependent in HIV infection. AICD can be blocked by ICE inhibitors in some patients, and this AICD is mediated by TRAIL. These results show that TRAIL can be a mediator of AICD in T cells. These different mechanisms of peripheral blood T cell apoptosis may play different roles in the pathogenesis of HIV infection.

L6 ANSWER 11 OF 18 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 97463826 MEDLINE
DOCUMENT NUMBER: 97463826
TITLE: Contribution of Fas ligand to T cell-mediated hepatic injury in mice.
AUTHOR: Seino K; Kayagaki N; Takeda K; Fukao K; Okumura K; Yagita H
CORPORATE SOURCE: Department of Immunology, Juntendo University School of Medicine, Tokyo, Japan.
SOURCE: GASTROENTEROLOGY, (1997 Oct) 113 (4) 1315-22.
Journal code: FH3. ISSN: 0016-5085.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199712
AB BACKGROUND & AIMS: Fas has been implicated in liver damage. The aim of this study was to investigate the role of its ligand to induce hepatocyte death and liver damage in T cell-dependent hepatitis. METHODS: Fas ligand-mediated lysis of primary hepatocytes from C57BL/6 wild-type, Fas ligand-deficient gld, and Fas-deficient lpr mice and concanavalin A-induced hepatitis in these mice were assessed. RESULTS: Freshly isolated hepatocytes from wild-type or gld mice, but not those from lpr mice, were susceptible to Fas ligand-mediated lysis. When concanavalin A was intravenously administered into wild-type mice, they developed acute hepatic injury with massive degenerative changes in hepatocytes. In contrast, both gld and lpr mice had lower aminotransferase levels with milder histological changes. Reverse-transcription polymerase chain reaction and flow cytometric analysis showed that Fas ligand was induced in the liver shortly after the concanavalin A injection and was predominantly expressed on intrahepatic T cells. Administration of ***monoclonal*** ***antibody*** neutralizing mouse ***Fas*** ***ligand*** could ***reduce*** the aminotransferase increase. CONCLUSIONS: The results indicate that ***Fas*** ***ligand*** plays a role in the T cell-dependent hepatitis induced by concanavalin A administration.

L6 ANSWER 12 OF 18 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 97180151 MEDLINE
DOCUMENT NUMBER: 97180151
TITLE: Involvement of Fas-mediated apoptosis in the inhibitory effects of interferon-alpha in chronic myelogenous leukemia.
AUTHOR: Selleri C; Sato T; Del Vecchio L; Luciano L; Barrett A J; Rotoli B; Young N S; Maciejewski J P
CORPORATE SOURCE: Hematology Division, Federico II University Medical School, Naples, Italy.
SOURCE: BLOOD, (1997 Feb 1) 89 (3) 957-64.
Journal code: A8G. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199705
ENTRY WEEK: 19970503
AB Interferon-alpha (IFN-alpha) is an established treatment for chronic myelogenous leukemia (CML) in chronic phase, but the mechanism of its antileukemic activity is not clear. One possible mechanism of action might include the induction of apoptosis, and especially Fas-mediated cell killing may play an important role in the elimination of malignant cells. We investigated Fas receptor (Fas-R) expression and the consequences of Fas-R triggering in CML patients. Using two-color flow cytometry, we found a significantly higher number of Fas-R-expressing CD34+ cells in the bone marrow (BM) of CML patients compared with normal subjects. We have previously shown that IFN-gamma induces Fas-R expression on CD34+ cells; in this study, we investigated whether IFN-alpha induces Fas-R expression on CML progenitor cells. Dose-dependent induction of Fas-R expression was observed after IFN-alpha stimulation of CD34+ cells from CML BM. In methylcellulose culture, IFN-alpha alone at a therapeutic concentration showed only marginal antiproliferative effects on both normal and CML BM progenitors. In contrast, a ***Fas*** -R agonist, the anti-CD95 ***monoclonal*** ***antibody*** CH11, ***inhibited*** colony formation from normal progenitors, and the inhibition was even stronger on CML progenitors. When CML BM cells were cultured in the presence of IFN-alpha, Fas-R-mediated inhibition of colony growth was potentiated in a dose-dependent fashion, consistent with IFN-alpha induction of Fas-R expression. This functional effect did not require the presence of accessory cells, since similar results were obtained with purified CD34+ cells. In suspension cultures, we demonstrated that suppression of CML hematopoiesis by IFN-alpha and Fas-R agonist was exerted through Fas-R-mediated induction of apoptosis. Our findings suggest that the Fas-R/Fas-ligand system might be involved in the immunologic regulation of CML progenitor growth and that its effect can be amplified by IFN-alpha.

L6 ANSWER 13 OF 18 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 1998042470 MEDLINE
DOCUMENT NUMBER: 98042470
TITLE: Fas/Fas ligand interaction regulates cytotoxicity of CD4+ T cells against staphylococcal enterotoxin B-pulsed endothelial cells.
AUTHOR: Urayama S; Kawakami A; Matsuoka N; Tsuboi M; Nakashima T; Kawabe Y; Koji T; Eguchi K
CORPORATE SOURCE: First Department of Internal Medicine, Nagasaki University School of Medicine, Japan.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1997 Oct 29) 239 (3) 782-8.
Journal code: 9Y8. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199802
ENTRY WEEK: 19980204
AB Infiltration of activated CD4+ T cells and apoptosis of endothelial cells are present in the synovium of rheumatoid arthritis (RA). Using staphylococcal enterotoxin B (SEB) as an antigen, we examined the possible role of antigen (Ag)-dependent activation of CD4+ T cells by endothelial cells, in inducing endothelial cell apoptosis. The human endothelial cell line, EA.hy926 cells, was cultured with or without interferon-gamma (IFN-gamma) and further incubated with CD4+ T cells in the presence or absence of SEB. After this cocultivation, the cytotoxicity and Fas ligand (FasL) expression of CD4+ T cells were examined. A small percentage of EA.hy926 cells expressed HLA-DR and -DQ, and this expression was significantly augmented after IFN-gamma stimulation. Anti-Fas IgM-induced apoptosis was exhibited by both unstimulated and IFN-gamma-stimulated EA.hy926 cells. Cytotoxicity of CD4+ T cells toward SEB-pulsed unstimulated EA.hy926 cells was detected. Furthermore, when CD4+ T cells were incubated with IFN-gamma-stimulated, SEB-pulsed EA.hy926 cells with augmented HLA-DR and -DQ expression, this cytotoxicity was more significant. The addition of anti-HLA-DR and -DQ ***monoclonal*** ***antibodies*** (mAbs) or human ***Fas*** chimeric protein (hFas-Fc) ***reduced*** the cytotoxicity. FasL expression was induced in CD4+ T cells cocultured with SEB-pulsed EA.hy926 cells, especially when the EA.hy926 cells were IFN-gamma-stimulated. Furthermore, the addition of mAbs against CD54 and CD58 inhibited both the cytotoxicity and FasL expression of CD4+ T cells induced by SEB-pulsed EA.hy926 cells, indicating the importance of costimulatory molecules on EA.hy926 cells in activating CD4+ T cells. Our results suggest that CD4+ T cells are activated by endothelial cells in an Ag-dependent manner and subsequently express FasL, which induces Fas-mediated apoptosis of endothelial cells. This phenomenon may counteract the growth of RA synovium by inhibiting the proliferation of endothelial cells.

L6 ANSWER 14 OF 18 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 97115842 MEDLINE
DOCUMENT NUMBER: 97115842
TITLE: Glutathione levels and sensitivity to apoptosis are regulated by changes in transaldolase expression.
AUTHOR: Banki K; Hutter E; Colombo E; Gonchoroff N J; Perl A
CORPORATE SOURCE: Department of Pathology, State University of New York Health Science Center, College of Medicine, Syracuse, New York 13210, USA.
CONTRACT NUMBER: RO1 DK 49221 (NIDDK)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Dec 20) 271 (51) 32994-3001.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199703
ENTRY WEEK: 19970304
AB Transaldolase (TAL) is a key enzyme of the reversible nonoxidative branch of the pentose phosphate pathway (PPP) that is responsible for the generation of NADPH to maintain glutathione at a reduced state (GSH) and, thus, to protect cellular integrity from reactive oxygen intermediates (ROIs). Formation of ROIs have been implicated in certain types of apoptotic cell death. To evaluate the role of TAL in this process, Jurkat human T cells were permanently transfected with TAL expression vectors oriented in the sense or antisense direction. Overexpression of TAL resulted in a decrease in glucose 6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase activities and NADPH and GSH levels and rendered these cells highly susceptible to apoptosis induced by serum deprivation, hydrogen peroxide, nitric oxide, tumor necrosis factor-alpha, and anti- ***Fas*** ***monoclonal*** ***antibody*** . In addition, ***reduced*** levels of TAL resulted in increased glucose 6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase activities and increased GSH levels with inhibition of apoptosis in all five model systems. The effect of TAL expression on susceptibility to apoptosis through regulating the PPP and GSH production is consistent with an involvement of ROIs in each pathway tested. Production of ROIs in Fas-mediated cell death was further substantiated by measurement of intracellular ROI production with oxidation-sensitive fluorescent probes, by the protective effects of GSH precursor, N-acetyl cysteine, free radical spin traps 5,5-dimethyl-1-pyrroline-1-oxide and 3,3,5,5-tetramethyl-1-pyrroline-1-oxide, the antioxidants desferrioxamine, nordihydroguaiaretic acid, and Amytal, and by the enhancing effects of GSH depletion with buthionine sulfoximine. The results provide definitive evidence that TAL has a role in regulating the balance between the two branches of PPP and its overall output as measured by GSH production and thus influences sensitivity to cell death signals.

L6 ANSWER 15 OF 18 MEDLINE DUPLICATE 14

ACCESSION NUMBER: 97094869 MEDLINE
DOCUMENT NUMBER: 97094869
TITLE: Protease involvement in fodrin cleavage and phosphatidylserine exposure in apoptosis.
AUTHOR: Vanags D M; Porn-Ares M I; Coppola S; Burgess D H; Orrenius S
CORPORATE SOURCE: Institute of Environmental Medicine, Division of Toxicology, Karolinska Institutet, Box 210, S-171 77 Stockholm, Sweden.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Dec 6) 271 (49) 31075-85.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199703
ENTRY WEEK: 19970302
AB A detailed kinetic analysis of three extranuclear end points of apoptosis, phosphatidylserine exposure, alpha-fodrin degradation, and plasma membrane blebbing, was performed and compared with nuclear fragmentation and the activation of the interleukin-1beta-converting enzyme (ICE)-like proteases in Jurkat T lymphocytes stimulated by anti-Fas monoclonal antibody (anti-Fas mAb) and in monocytic U937 cells stimulated by tumor necrosis factor (TNF) and cycloheximide. Phosphatidylserine exposure was quantitated by plasma clotting time, as well as annexin V-fluorescein isothiocyanate binding, and the ICE-like protease activity was examined by the cleavage of a specific fluorogenic peptide substrate Ac-Asp-Glu-Val-Asp-amino-4-methylcoumarin. VAD-chloromethylketone (VAD-cmk), an inhibitor of ICE-like proteases, effectively inhibited ICE-like activity in both cell types studied, whereas the calpain inhibitor calpeptin was ineffective. VAD-cmk also effectively inhibited all three extranuclear events, as well as nuclear fragmentation, in Jurkat cells stimulated by anti-Fas monoclonal antibody, indicating that ICE-like proteases play an important role in the regulation of this apoptotic system. Calpain inhibitors were ineffective in this system. TNF-induced extranuclear and nuclear changes in U937 cells were inhibited by calpeptin but were not as effectively inhibited by VAD-cmk as in Jurkat cells. This suggests that ICE-like enzymes predominate in anti- ***Fas*** ***monoclonal*** ***antibody*** -stimulated Jurkat cells, whereas proteases affected by calpain ***inhibitors*** as well as the ICE-like enzymes are involved in the signaling of apoptotic events in TNF-induced U937 cells. Importantly, the two apoptotic systems seem to be regulated by different proteases.

L6 ANSWER 16 OF 18 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 96406522 MEDLINE
DOCUMENT NUMBER: 96406522
TITLE: Extensive apoptosis of lung T-lymphocytes maintained in vitro.
AUTHOR: Herry I; Bonay M; Bouchonnet F; Schuller M P; Lecossier D; Tazi A; Lynch D H; Hance A J
CORPORATE SOURCE: INSERM U.82, Faculte de Medecine Xavier Bichat, Paris, France.
SOURCE: AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR
BIOLOGY, (1996 Sep) 15 (3) 339-47.
Journal code: AOB. ISSN: 1044-1549.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY WEEK: 19970104
AB The phenotypic and functional properties of T cells recovered from the lung indicate that many of these cells have been recently activated. Because such recently activated cells are often more susceptible to death through apoptotic mechanisms, the viability of lung T cells recovered from bronchoalveolar lavage and those isolated from peripheral blood was compared. The progressive loss of viable cells following in vitro culture was considerably greater for lavage T cells than blood T cells, and was observed for cells from both patients with sarcoidosis and control subjects. Following 4 days of culture, 76 +/- 14% of blood cells, but only 31 +/- 13% of lavage cells from sarcoid patients were viable. The evaluation of morphologic features and flow cytometric profiles, as well as the demonstration of typical oligonucleosomal fragmentation of DNA extracted from these cells indicated that lavage T cells were dying by apoptotic mechanisms. CD4+ T cells appeared to be particularly sensitive to apoptosis. Most lavage T cells from controls and sarcoid patients expressed Fas (CD95) antigen. Although some lavage T Cells were sensitive to Fas-induced apoptosis, the viability of lavage T cells was not improved by incubation in the presence of a ***monoclonal*** ***antibody*** that ***inhibits*** ***Fas*** -induced apoptosis. Culture in the presence of interleukin 2 did prevent, at least in part, the progressive death of lavage T cells, suggesting that the viability of T cells in the lung may depend on the presence of locally delivered trophic signals. These studies emphasize that T cells on the alveolar surface are in a different state of activation and differentiation compared with that of circulating T cells, and offer a possible explanation for the impaired functional capacities observed for lavage T cells in some in vitro studies.

L6 ANSWER 17 OF 18 PATOSWO COPYRIGHT 1998 WILA
WOA1 PCT-PUBLICATION
ABEN The present invention provides a panel of monoclonal antibodies and binding proteins which specifically bind to human Fas antigen. Some of the antibodies and binding proteins are capable of stimulating T cell proliferation, ***inhibiting*** binding of anti- ***Fas*** CH-11 ***monoclonal*** ***antibody*** to cells expressing Fas antigen, blocking anti-Fas CH-11 monoclonal antibody-mediated lysis of cells, and blocking Fas ligand-mediated lysis of cells. The invention also provides for therapeutic compositions comprising the monoclonal antibodies.

L6 ANSWER 18 OF 18 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 95297129 MEDLINE
DOCUMENT NUMBER: 95297129
TITLE: Activation of the apoptotic Fas antigen-encoding gene upon influenza virus infection involving spontaneously produced beta-interferon.
AUTHOR: Takizawa T; Fukuda R; Miyawaki T; Ohashi K; Nakanishi Y
CORPORATE SOURCE: Department of Biochemistry, Aichi Human Service Center, Japan.
SOURCE: VIROLOGY, (1995 Jun 1) 209 (2) 288-96.
Journal code: XEA. ISSN: 0042-6822.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199509
AB We previously demonstrated that influenza virus infection induces apoptosis in culture cells. Here, we examined the activation of the Fas antigen gene that encodes an apoptosis-mediating membrane protein in the virus-infected cells. The virus elicited a transient but marked increase in Fas antigen mRNA 3 to 4 hr after infection, followed by the expression of the antigen on the cell surface. Poly(I)-poly(C), a synthetic double-stranded RNA, similarly activated Fas antigen gene expression, and poly(I)-poly(C)-treated cells are highly susceptible to the cell killing effect of IgM isotype of anti-Fas ***monoclonal*** ***antibody*** . On the other hand, the IgG isotype of anti- ***Fas*** ***monoclonal*** ***antibody*** , which has an ***inhibitory*** effect on ***Fas*** Ag-mediated cell death, suppressed the virus-induced cell death. Prior exposure of the cells to anti-interferon-beta antibody decreased the degree of cell death as well as the amount of Fas mRNA. The autophosphorylation activity of double-stranded RNA-activated protein kinase was also decreased in the antibody-treated cells. Moreover, a protein kinase inhibitor, 2-aminopurine, blocked the Fas Ag gene activation by poly(I)-poly(C). These results suggested that the activation of Fas Ag gene in the early phase of infection is an important event for apoptosis, and that it is regulated by the double-stranded RNA/interferon system involving protein phosphorylation.

=> d his

(FILE 'HOME' ENTERED AT 14:15:55 ON 07 MAY 1998)

FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, PATOSWO' ENTERED AT 14:16:45 ON 07 MAY 1998
L1 2798 S FAS(W)LIGAND OR FAS(W)SUBSTRATE
L2 5150812 S (INHIBIT? OR REDUC? OR ANTAGON?)
L3 413230 S MONOCLONAL(W)ANTIBOD?
L4 13464 S FAS
L5 62 S (L1 OR L4)(10A)L2(10A)L3
L6 18 DUP REM L5 (44 DUPLICATES REMOVED)

=> logoff

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	104.38	104.68

STN INTERNATIONAL LOGOFF AT 14:30:49 ON 07 MAY 1998

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 ********************************
FILE 'USPAT' ENTERED AT 14:32:22 ON 07 MAY 1998

 ********************************
 *      WELCOME TO THE          *
 *   U.S. PATENT TEXT FILE      *
 ********************************

=> file uspat jpo epo

FILE 'USPAT' ENTERED AT 14:33:15 ON 07 MAY 1998

 ********************************
 *      WELCOME TO THE          *
 *   U.S. PATENT TEXT FILE      *
 ********************************

FILE 'JPO' ENTERED AT 14:33:15 ON 07 MAY 1998

 ********************************
          G P I                 *
   JAPANESE PATENT ABSTRACTS    *
    ********************************


FILE 'EPO' ENTERED AT 14:33:15 ON 07 MAY 1998

 ********************************
 *          G P I               *
 *  EUROPEAN PATENT ABSTRACTS   *
 ********************************


=> s fas

FILE 'USPAT'
L1      511 FAS

FILE 'JPO'
L2       95 FAS

FILE 'EPO'
L3       32 FAS

TOTAL FOR ALL FILES
L4      638 FAS

=> s inhib? or reduc? or suppress? or antagon?

FILE 'USPAT'
      249775 INHIB?
     1318072 REDUC?
      117950 SUPPRESS?
       18619 ANTAGON?
L5    1400039 INHIB? OR REDUC? OR SUPPRESS? OR ANTAGON?

FILE 'JPO'
       50917 INHIB?
      662994 REDUC?
      125717 SUPPRESS?
        1509 ANTAGON?
L6     803500 INHIB? OR REDUC? OR SUPPRESS? OR ANTAGON?

FILE 'EPO'
       34947 INHIB?
      170282 REDUC?
       13175 SUPPRESS?
        4922 ANTAGON?
L7     216498 INHIB? OR REDUC? OR SUPPRESS? OR ANTAGON?

TOTAL FOR ALL FILES
L8    2420037 INHIB? OR REDUC? OR SUPPRESS? OR ANTAGON?

=> s monoclonal(w)antibod?

FILE 'USPAT'
      12509 MONOCLONAL
      27885 ANTIBOD?
L9    11553 MONOCLONAL(W)ANTIBOD?

FILE 'JPO'
       1801 MONOCLONAL
       5761 ANTIBOD?
L10    1742 MONOCLONAL(W)ANTIBOD?

FILE 'EPO'
       2827 MONOCLONAL
       9133 ANTIBOD?
L11    2614 MONOCLONAL(W)ANTIBOD?

TOTAL FOR ALL FILES
L12   15909 MONOCLONAL(W) ANTIBOD?

=> s l4(10a)l8(10a)l12

FILE 'USPAT'
L13       1 L1(10A)L5(10A)L9

FILE 'JPO'
L14       1 L2(10A)L6(10A)L10

FILE 'EPO'
L15       2 L3(10A)L7(10A)L11

TOTAL FOR ALL FILES
L16       4 L4(10A) L8(10A) L12

=> d l16 1-4 leg ab


US PAT NO:  5,620,889 [IMAGE AVAILABLE]     L16: 1 of 4
DATE ISSUED:  Apr. 15, 1997
TITLE:  Human anti-Fas IgG1 monoclonal antibodies
INVENTOR:  David H. Lynch, Bainbridge Island, WA
           Mark R. Alderson, Bainbridge Island, WA
ASSIGNEE:  Immunex Corporation, Seattle, WA (U.S. corp.)
APPL-NO:  08/322,805
DATE FILED:  Oct. 13, 1994
ART-UNIT:  186
PRIM-EXMR:  Susan A. Loring

US PAT NO:  5,620,889 [IMAGE AVAILABLE]     L16: 1 of 4

ABSTRACT:
The present invention provides a panel of monoclonal antibodies and
binding proteins which specifically bind to human Fas antigen. Some of
the antibodies and binding proteins are capable of stimulating T cell
proliferation, **inhibiting** binding of anti-**Fas** CH-11
**monoclonal** **antibody** to cells expressing Fas antigen, blocking
anti-Fas CH-11 monoclonal antibody-mediated lysis of cells, and blocking
Fas ligand-mediated lysis of cells. The invention also provides for
therapeutic compositions comprising the monoclonal antibodies.

DISPLAY DATA FOR THIS FILE IS TEMPORARILY UNAVAILABLE

EP000709097A1                               L16: 3 of 4

ABSTRACT:

   The present invention relates to a therapeutic agent for rheumatic
disease comprising an anti-Fas **monoclonal** **antibody**, or the
combination of an anti-**Fas** **monoclonal** **antibody** and a medical
substance having an **inhibitory** effect of cell proliferation as an
active ingredient. The anti-**Fas** **monoclonal** **antibody** of this
invention reacts with the Fas antigen in synovial cells of patients with
rheumatoid arthritis, especially the human Fas antigen specifically and
expresses apoptosis on synovial cells. <IMAGE>

WO0009510540A1                              L16: 4 of 4

ABSTRACT:

<CHG DATE=19950607 STATUS=O>The present invention provides a panel of
monoclonal antibodies and binding proteins which specifically bind to
human Fas antigen. Some of the antibodies and binding proteins are
capable of stimulating T cell proliferation, **inhibiting** binding of
anti-**Fas** CH-11 **monoclonal** **antibody** to cells expressing Fas
antigen, blocking anti-Fas CH-11 monoclonal antibody-mediated lysis of
cells, and blocking Fas ligand-mediated lysis of cells. The invention
also provides for therapeutic compositions comprising the monoclonal
antibodies.

=> d l16 1-4


1. 5,620,889, Apr. 15, 1997, Human anti-Fas IgG1 monoclonal antibodies;
David H. Lynch, et al., 435/332; 424/144.1; 435/334, 343.2; 530/387.1,
388.2, 388.23, 388.24, 388.75 [IMAGE AVAILABLE]

DISPLAY DATA FOR THIS FILE IS TEMPORARILY UNAVAILABLE

3. EP000709097A1, May 1, 1996, Anti-Fas antibody for rheumatic disease;
NISHIOKA, KUSIKI (JP), et al.,
INT-CL:  [6] A61K39/395
EUR-CL:  A61K39/395; C07K16/28

4. WO0009510540A1, Apr. 20, 1995, FAS ANTAGONISTS AND USES THEREOF;
LYNCH, DAVID H, et al.,
INT-CL:  [6] C07K16/28; [6] A61K39/395
EUR-CL:  C07K16/28

=> s l4(20a)l8(20a)l12

FILE 'USPAT'
L17       1 L1(20A)L5(20A)L9

FILE 'JPO'
L18       1 L2(20A)L6(20A)L10

FILE 'EPO'
L19       2 L3(20A)L7(20A)L11

TOTAL FOR ALL FILES
L20       4 L4(20A) L8(20A) L12

=> d l20 1-4


1. 5,620,889, Apr. 15, 1997, Human anti-Fas IgG1 monoclonal antibodies;
David H. Lynch, et al., 435/332; 424/144.1; 435/334, 343.2; 530/387.1,
388.2, 388.23, 388.24, 388.75 [IMAGE AVAILABLE]

DISPLAY DATA FOR THIS FILE IS TEMPORARILY UNAVAILABLE

3. EP000709097A1, May 1, 1996, Anti-Fas antibody for rheumatic disease;
NISHIOKA, KUSIKI (JP), et al.,
INT-CL:  [6] A61K39/395
EUR-CL:  A61K39/395; C07K16/28

4. WO0009510540A1, Apr. 20, 1995, FAS ANTAGONISTS AND USES THEREOF;
LYNCH, DAVID H, et al.,
INT-CL:  [6] C07K16/28; [6] A61K39/395
EUR-CL:  C07K16/28

=> s l4 and l8 and l12

FILE 'USPAT'
L21       48 L1 AND L5 AND L9

FILE 'JPO'
L22        2 L2 AND L6 AND L10
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FILE 'EPO'
L23 2 L3 AND L7 AND L11

TOTAL FOR ALL FILES
L24 52 L4 AND L8 AND L12

=> d l24 1-52 bib ab

US PAT NO: 5,747,245 [IMAGE AVAILABLE] L24: 1 of 52
DATE ISSUED: May 5, 1998
TITLE: Nucleic acids encoding **Fas** associated proteins and screening assays using same
INVENTOR: John C. Reed, Carlsbad, CA
Takaaki Sato, San Diego, CA
ASSIGNEE: La Jolla Cancer Research Foundation, La Jolla, CA (U.S. corp.)
APPL-NO: 08/259,514
DATE FILED: Jun. 14, 1994
ART-UNIT: 187
PRIM-EXMR: Stephanie W. Zitomer
ASST-EXMR: Dianne Rees

US PAT NO: 5,747,245 [IMAGE AVAILABLE] L24: 1 of 52

ABSTRACT:
The present invention provides mammalian protein tyrosine phosphatases, human PTP-BAS type 4, human PTP-BAS type 5a and mouse PTP-BAS type 5b, each of which is a **Fas**-associated protein (FAP), nucleic acid molecules encoding a PTP-BAS type 4 or a PTP-BAS type 5 and antibodies specific for a PTP-BAS type 4 or for a PTP-BAS type 5. The invention also provides methods for identifying FAP's, which can associate with **Fas** and can modulate apoptosis. The invention also provides screening assays for identifying an agent that can effectively alter the association of a FAP with **Fas** and, therefore, can increase or decrease the level of apoptosis in a cell. The invention further provides methods of modulating apoptosis in a cell by introducing into the cell a nucleic acid molecule encoding a PTP-BAS or an antisense nucleotide sequence, which is complementary to a portion of a nucleic acid molecule encoding a PTP-BAS. The invention also provides a method of using a reagent that can specifically bind to a FAP to diagnose a pathology that is characterized by an increased or decreased level of apoptosis in a cell. The invention also provides methods of modulating apoptosis in a cell by contacting the cell with an agent that effectively alters the association of a FAP and **Fas** in a cell or alters the activity of a FAP in a cell.

US PAT NO: 5,741,667 [IMAGE AVAILABLE] L24: 2 of 52
DATE ISSUED: Apr. 21, 1998
TITLE: Tumor necrosis factor receptor-associated factors
INVENTOR: David V. Goeddel, Hillsborough, CA
Mike Rothe, San Mateo, CA
ASSIGNEE: Genentech, Inc., South San Francisco, CA (U.S. corp.)
APPL-NO: 08/446,915
DATE FILED: May 22, 1995
ART-UNIT: 182
PRIM-EXMR: John Ulm
LEGAL-REP: Ginger R. Dreger

US PAT NO: 5,741,667 [IMAGE AVAILABLE] L24: 2 of 52

ABSTRACT:
The invention concerns new tumor necrosis factor receptor associated factors, designated TRAFs. The new factors are capable of specific association with the intracellular domain of the type 2 TNF receptor (TNF-R2) and CD40, and are involved in the mediation of TNF and CD40 ligand biological activities.

US PAT NO: 5,733,904 [IMAGE AVAILABLE] L24: 3 of 52
DATE ISSUED: Mar. 31, 1998
TITLE: Method for prevention and treatment of viral infectious diseases for viral **suppression**
INVENTOR: Yoichi Fujii, Nagoya, Japan
Akio Adachi, Tokushima, Japan
Toshio Asano, Mishima, Japan
ASSIGNEE: Asahi Kasei Kogyo Kabushiki Kaisha, Osaka, Japan (foreign corp.)
APPL-NO: 08/815,669
DATE FILED: Mar. 10, 1997
ART-UNIT: 125
PRIM-EXMR: Jerome D. Goldberg
LEGAL-REP: Young & Thompson

US PAT NO: 5,733,904 [IMAGE AVAILABLE] L24: 3 of 52

ABSTRACT:
A method for prevention and treatment of viral infectious diseases using a medicament containing an effective amount of a compound of the formula ##STR1## where R.sup.1 is hydrogen or hydroxy, or acid addition salt thereof.

US PAT NO: 5,733,738 [IMAGE AVAILABLE] L24: 4 of 52
DATE ISSUED: Mar. 31, 1998
TITLE: Polypeptide-induced monoclonal receptors to protein ligands
INVENTOR: Henry L. Niman, Carlsbad, CA
ASSIGNEE: Ligand Pharmaceuticals, San Diego, CA (U.S. corp.)
APPL-NO: 08/418,898
DATE FILED: Apr. 7, 1995
ART-UNIT: 186
PRIM-EXMR: David Saunders
LEGAL-REP: Lyon & Lyon LLP

US PAT NO: 5,733,738 [IMAGE AVAILABLE] L24: 4 of 52

ABSTRACT:
The present invention relates to immunological receptors and ligands, and more particularly to monoclonal receptors raised to peptides whose amino acid residue sequences correspond to sequences of retroviral ligands. The receptors are used to assay body samples from a host to indicate exposure of the host to a carcinogen.

US PAT NO: 5,726,286 [IMAGE AVAILABLE] L24: 5 of 52
DATE ISSUED: Mar. 10, 1998
TITLE: Isolated epstein-barr virus BZLF2 proteins that bind MHC class II beta chains
INVENTOR: Mark Alderson, Bainbridge Island, WA
Richard J. Armitage, Bainbridge Island, WA
Jeffrey I. Cohen, SIlver Spring, MD
Michael R. Comeau, Seattle, WA
Theresa M. Farrah, Seattle, WA
Lindsey M. Hutt-Fletcher, Kansas City, MO
Melanie K. Spriggs, Seattle, WA
ASSIGNEE: Immunex Corporation, Seattle, WA (U.S. corp.)
APPL-NO: 08/430,633
DATE FILED: Apr. 28, 1995
ART-UNIT: 185
PRIM-EXMR: Marian C. Knode
ASST-EXMR: Ali R. Salimi
LEGAL-REP: Patricia Anne Perkins

US PAT NO: 5,726,286 [IMAGE AVAILABLE] L24: 5 of 52

ABSTRACT:
Isolated viral proteins, and pharmaceutical compositions made therefrom, are disclosed which are capable of binding to a .beta. chain of a Class II Major Histocompatibility Complex antigen, thereby functioning to **inhibit** an antigen-specific response. The viral proteins also have superantigen-like activity, and **inhibit** EBV infection.

US PAT NO: 5,714,667 [IMAGE AVAILABLE] L24: 6 of 52
DATE ISSUED: Feb. 3, 1998
TITLE: Mice lacking expression of CTLA-4 receptor
INVENTOR: Paul David Waterhouse, London, Canada
Tak Wah Mak, Toronto, Canada
ASSIGNEE: Amgen Canada Inc., Mississauga, Canada (foreign corp.)
APPL-NO: 08/554,133
DATE FILED: Nov. 6, 1995
ART-UNIT: 189
PRIM-EXMR: Jasemine C. Chambers, PHD.
ASST-EXMR: Jill D. Schmuck
LEGAL-REP: Nancy A. Oleski, Ron Levy, Steven M. Odre

US PAT NO: 5,714,667 [IMAGE AVAILABLE] L24: 6 of 52

ABSTRACT:
Disclosed is a mouse in which expression of the gene encoding the CTLA-4 receptor is **suppressed**. Also disclosed is a nucleic acid construct useful in preparing such a mouse, and a cell line containing such construct.

US PAT NO: 5,712,381 [IMAGE AVAILABLE] L24: 7 of 52
DATE ISSUED: Jan. 27, 1998
TITLE: MADD, a TNF receptor death domain ligand protein
INVENTOR: Lih-Ling Lin, Concord, MA
Jennifer Chen, Chestnut Hill, MA
Andrea R. Schievella, Winchester, MA
James Graham, Somerville, MA
ASSIGNEE: Genetics Institute, Inc., Cambridge, MA (U.S. corp.)
APPL-NO: 08/698,551
DATE FILED: Aug. 15, 1996
ART-UNIT: 182
PRIM-EXMR: Stephen Walsh
ASST-EXMR: Mukul Ranjan
LEGAL-REP: Scott A. Brown, Suzanne A. Sprunger, Thomas J. DesRosier

US PAT NO: 5,712,381 [IMAGE AVAILABLE] L24: 7 of 52

ABSTRACT:
Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are also disclosed, along with vectors, host cells, and methods of making the TNF-R1-DD ligand protein. Pharmaceutical compositions containing the TNF-R1-DD ligand protein, methods of treating inflammatory conditions, and methods of **inhibiting** TNF-R death domain binding are also disclosed. Methods of identifying **inhibitors** of TNF-R death domain binding and **inhibitors** identified by such methods are also disclosed.

US PAT NO: 5,712,115 [IMAGE AVAILABLE] L24: 8 of 52
DATE ISSUED: Jan. 27, 1998
TITLE: Human cell death-associated protein
INVENTOR: Phillip R. Hawkins, Mountain View, CA
Scott Michael Braxton, San Mateo, CA
Lynn E. Murry, Portola Valley, CA
ASSIGNEE: Incyte Pharmaceuticals, Inc., Palo Alto, CA (U.S. corp.)
APPL-NO: 08/618,164
DATE FILED: Mar. 19, 1996
ART-UNIT: 186
PRIM-EXMR: Christina Y. Chan
ASST-EXMR: Emma Cech
LEGAL-REP: Lucy J. Billings, Barbara J. Luther

US PAT NO: 5,712,115 [IMAGE AVAILABLE] L24: 8 of 52

ABSTRACT:
The present invention provides a polynucleotide which identifies and encodes a human cell death-associated protein (cdap) which was isolated from a rheumatoid synovium library. The invention provides for genetically engineered expression vectors and host cells comprising a nucleic acid sequence encoding CDAP. The invention also provides for the therapeutic use of purified CDAP, cdap or its antisense molecules, or CDAP **inhibitors** in pharmaceutical compositions and for treatment of conditions or diseases associated with expression of CDAP. The invention also describes diagnostic assays which utilize diagnostic compositions comprising the polynucleotide, or fragments thereof, or antibodies which specifically bind to the polypeptide.

US PAT NO: 5,705,380 [IMAGE AVAILABLE] L24: 9 of 52
DATE ISSUED: Jan. 6, 1998
TITLE: Identification of a gene encoding TULP2, a retina specific protein
INVENTOR: Michael North, San Diego, CA
Patsy Nishina, Bar Harbor, ME
Juergen Naggert, Bar Harbor, ME
ASSIGNEE: Sequana Theraputics, Inc., La Jolla, CA (U.S. corp.)
Jackson Lab., Bar Harbor, ME (U.S. corp.)
APPL-NO: 08/706,292
DATE FILED: Sep. 4, 1996
ART-UNIT: 187
PRIM-EXMR: W. Gary Jones
ASST-EXMR: Debra Shoemaker
LEGAL-REP: PamelaBozicevic & Reed, LLP. Sherwood, Ph. D.

US PAT NO: 5,705,380 [IMAGE AVAILABLE] L24: 9 of 52

ABSTRACT:
The gene responsible for an autosomal dominant con-rod retinal dystrophy is identified, TULP2. The genes are used to produce the encoded protein; screening for compositions that modulate the expression or function of TULP2 protein; and in studying associated physiological pathways.

US PAT NO: 5,702,897 [IMAGE AVAILABLE] L24: 10 of 52
DATE ISSUED: Dec. 30, 1997
TITLE: Interaction of proteins involved in a cell death pathway
INVENTOR: John C. Reed, Carlsbad, CA
Takaaki Sato, San Diego, CA
ASSIGNEE: The Burnham Institute, La Jolla, CA (U.S. corp.)
APPL-NO: 08/607,269
DATE FILED: Feb. 20, 1996
ART-UNIT: 185
PRIM-EXMR: James Ketter
LEGAL-REP: Campbell & Flores LLP

US PAT NO: 5,702,897 [IMAGE AVAILABLE] L24: 10 of 52

ABSTRACT:
The present invention provides methods for detecting an interaction among proteins involved in regulating cell death. The invention also provides a drug screening assay useful for identifying agents that alter an interaction among proteins involved in controlling cell death. The invention further provides a method for identifying novel proteins that are involved in a cell death pathway.

US PAT NO: 5,698,520 [IMAGE AVAILABLE] L24: 11 of 52
DATE ISSUED: Dec. 16, 1997
TITLE: Peptide related to human programmed cell death and DNA encoding the same
INVENTOR: Tasuku Honjo, Kan'yuchi, Kitashirakawa Oiwakecho, Sakyo-ku, Kyoto, Japan
Yasumasa Ishida, Newton, MA
Takashi Shinohara, Kyoto, Japan
ASSIGNEE: Ono Pharmaceutical Co., Ltd., Osaka, Japan (foreign corp.)
Tasuku Honjo, Kyoto, Japan (foreign indiv.)
APPL-NO: 08/768,626
DATE FILED: Dec. 18, 1996
ART-UNIT: 184
PRIM-EXMR: Rebecca E. Prouty
ASST-EXMR: Gabriele E. Bugaisky
LEGAL-REP: Sughrue, Mion, Zinn, Macpeak & Seas, PLLC

US PAT NO: 5,698,520 [IMAGE AVAILABLE] L24: 11 of 52

ABSTRACT:
A membrane protein related to human programmed cell death (PD-1) and DNA encoding the said protein is provided. PD-1 protein may be useful for the treatment of various infections, immunological depression or acceleration, or tumors etc.

US PAT NO: 5,698,443 [IMAGE AVAILABLE] L24: 12 of 52
DATE ISSUED: Dec. 16, 1997
TITLE: Tissue specific viral vectors
INVENTOR: Daniel Robert Henderson, Palo Alto, CA
Eric Rodolph Schuur, Cupertino, CA
ASSIGNEE: Calydon, Inc., Menlo Park, CA (U.S. corp.)
APPL-NO: 08/495,034
DATE FILED: Jun. 27, 1995
ART-UNIT: 184
PRIM-EXMR: Jacqueline M. Stone
ASST-EXMR: Andrew K. Milne

US PAT NO: 5,698,443 [IMAGE AVAILABLE] L24: 12 of 52

ABSTRACT:
Host cell specific adenovirus vehicles are provided for transfecting target host cells. By providing for transcriptional initiating regulation dependent upon transcription factors that are only active in specific, limited cell types, virus replication will be restricted to the target cells. The modified adenovirus may be used as a vehicle for introducing new genetic capability, particularly associated with cytotoxicity for treating neoplasia.

US PAT NO: 5,686,598 [IMAGE AVAILABLE] L24: 13 of 52
DATE ISSUED: Nov. 11, 1997
TITLE: Genes associated with retinal dystrophies
INVENTOR: Michael North, San Diego, CA
Patsy Nishina, Bar Harbor, ME
Juergen Naggert, Bar Harbor, ME
ASSIGNEE: The Jackson Laboratory, Bar Harbor, ME (U.S. corp.)
Sequana Therapeutics, Inc., La Jolla, CA (U.S. corp.)
APPL-NO: 08/701,380
DATE FILED: Aug. 22, 1996
ART-UNIT: 186
PRIM-EXMR: Christina Y. Chan
ASST-EXMR: F. Pierre VanderVegt
LEGAL-REP: Pamela J. Sherwood

US PAT NO: 5,686,598 [IMAGE AVAILABLE] L24: 13 of 52

ABSTRACT:
The gene responsible for the autosomal recessive retinal degenerative disease RP 14 is identified, TULP1. The genes are used to produce the encoded protein; in screening for compositions that modulate the expression or function of TULP1 protein; and in studying associated physiological pathways. The DNA is further used as a diagnostic for genetic predisposition to retinal degeneration.

US PAT NO: 5,686,583 [IMAGE AVAILABLE] L24: 14 of 52
DATE ISSUED: Nov. 11, 1997
TITLE: Specific antibodies against activated platelets, the preparation thereof and the use thereof in diagnosis and therapy
INVENTOR: Klaus Bosslet, Marburg, Federal Republic of Germany
Gerhard Seemann, Marburg-Elnhausen, Federal Republic of Germany
Beate Kehrel, Munster, Federal Republic of Germany
ASSIGNEE: Behringwerke Aktiengesellschaft, Marburg, Federal Republic of Germany (foreign corp.)
APPL-NO: 08/467,393
DATE FILED: Jun. 6, 1995
ART-UNIT: 186
PRIM-EXMR: Frank C. Eisenschenk
LEGAL-REP: Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.

US PAT NO: 5,686,583 [IMAGE AVAILABLE] L24: 14 of 52

ABSTRACT:
The invention relates to **monoclonal** **antibodies** and parts thereof which bind preferentially to active human platelets, to the nucleotide sequence and amino-acid sequence of the heavy and light chain of MAb BW 2128 and to an antigen associated with thrombospondin.

US PAT NO: 5,686,072 [IMAGE AVAILABLE] L24: 15 of 52
DATE ISSUED: Nov. 11, 1997
TITLE: Epitope-specific **monoclonal** **antibodies** and immunotoxins and uses thereof
INVENTOR: Jonathan W. Uhr, Dallas, TX
Ellen S. Vitetta, Dallas, TX
Richard H. Scheuermann, Carrollton, TX
ASSIGNEE: Board of Regents, The University of Texas, Austin, TX (U.S. corp.)
APPL-NO: 08/202,042
DATE FILED: Feb. 22, 1994
ART-UNIT: 186
PRIM-EXMR: Toni R. Scheiner
LEGAL-REP: Arnold White & Durkee

US PAT NO: 5,686,072 [IMAGE AVAILABLE] L24: 15 of 52

ABSTRACT:
The anti-tumor activity of a mixture of anti-CD22 and anti-CD19 immunotoxins is shown to be significantly enhanced in SCID/Daudi mice with disseminated human Daudi lymphoma. Unexpectedly identical enhancement was observed employing a combination of the anti-CD22 immunotoxin with unconjugated anti-CD19 antibodies. Thus combinations of an anti-CD22 immunotoxin and an anti-CD19 immunotoxin or antibody act synergistically and provide advantageous compositions and methods for immunotherapeutic treatment of various diseases including cancer and autoimmune disorders. Also disclosed is data indicating that certain anti-CD19 antibodies alone **inhibit** proliferation of CD19-positive cells by inducing cell cycle arrest.

US PAT NO: 5,684,222 [IMAGE AVAILABLE] L24: 16 of 52
DATE ISSUED: Nov. 4, 1997
TITLE: Mutant mouse having a disrupted TNFRp55
INVENTOR: Tak W. Mak, Toronto, Canada
ASSIGNEE: Ontario Cancer Institute, Toronto, Canada (foreign corp.)
APPL-NO: 08/274,122
DATE FILED: Jul. 12, 1994
ART-UNIT: 184
PRIM-EXMR: Brian R. Stanton
LEGAL-REP: Marshall, O'Toole, Gerstein, Murray & Borun

US PAT NO: 5,684,222 [IMAGE AVAILABLE] L24: 16 of 52

ABSTRACT:
The multiple biological activities of tumor necrosis factor (TNF) are mediated by two distinct cell surface receptors of 55 and 75 kDa. Mutant mice of the invention lacking tumor necrosis factor receptor (TNFR) p55 still express functional TNFRp75 molecules at the cell surface. Normal weight and size of the mutant mice are not altered. Thymocyte development and lymphocyte populations are normal, and clonal deletion of potentially self-reactive T cells is not impaired. Activation of the nuclear transcription factor .kappa.B (NF-.kappa.B), however, is completely abrogated after stimulation with TNF. Moreover, TNFRp55 mutant mice are protected from septic shock induced by bacterial endotoxin or superantigen, but Listeria clearance is severely impaired and mutant mice easily succumb to Listeria infection. Thus, the two TNF receptors are not redundant, are independently controlled, and play different roles in normal and pathological physiology.

US PAT NO: 5,684,136 [IMAGE AVAILABLE] L24: 17 of 52
DATE ISSUED: Nov. 4, 1997
TITLE: Chimeric hepatocyte growth factor (HGF) ligand variants
INVENTOR: Paul J. Godowski, Burlingame, CA
ASSIGNEE: Genentech, Inc., South San Francisco, CA (U.S. corp.)
APPL-NO: 08/435,501
DATE FILED: May 5, 1995
ART-UNIT: 188
PRIM-EXMR: Marianne P. Allen
ASST-EXMR: Robert C. Hayes
LEGAL-REP: Diane L. Marschang, Deirdre L. Conley

US PAT NO: 5,684,136 [IMAGE AVAILABLE] L24: 17 of 52

ABSTRACT:
The invention concerns a method for activating receptors selected from receptor tyrosine kinases, cytokine receptors and members of the nerve growth factor receptor superfamily. A conjugate comprising the direct fusion of at least two ligands capable of binding to the receptor(s) to be activated is contacted with the receptors, whereby the ligands bind their respective receptors inducing receptor oligomerization.

US PAT NO: 5,675,060 [IMAGE AVAILABLE] L24: 18 of 52
DATE ISSUED: Oct. 7, 1997
TITLE: Transgenic arthritic mice expressing a T-cell receptor transgene
INVENTOR: Christophe O. Benoist, Strasbourg, France
Diane J. Mathis, Strasbourg, France
Valerie Kouskoff, Denver, CO
ASSIGNEE: Institut National de la Sante et de la Recherche Medicale, Paris, France (foreign corp.)
Centre National de la Recherche Scientifique, Paris, France (foreign govt.)
Universite Louis Pasteur, Strasbourg 1, Paris, France (foreign corp.)
E.R. Squibb & Sons, Inc., Princeton, NJ (U.S. corp.)
APPL-NO: 08/246,242
DATE FILED: May 19, 1994
ART-UNIT: 184
PRIM-EXMR: Deborah Crouch
LEGAL-REP: Sterne, Kessler, Goldstein & Fox, P.L.L.C.

US PAT NO: 5,675,060 [IMAGE AVAILABLE] L24: 18 of 52

ABSTRACT:
A transgenic animal model for arthritis is disclosed. The arthritic condition results from genetic (or immunologic) manipulations that result in the T cell receptor (TCR) repertoire of the animal being substantially limited relative to the TCR repertoire of a wildtype control animal. The TCR repertoire of the arthritic animal, albeit limited, is functionally viable. In a preferred embodiment, the invention relates to transgenic arthritic mice wherein arthritis results from (1) a transgenic allele which encodes and expresses TCR .alpha. and .beta. subunits that combine in T lymphocytes of the transgenic animal to form a TCR that recognizes an antigen comprising one or more epitopes of an oligopeptide derived from amino acids 41-61 of bovine pancreatic ribonuclease and/or (2) polypeptide arthritogenic self antigens derived from endogenous proteins. The transgenic arthritic mice of the invention provides an animal model which faithfully mimics rheumatoid arthritis and by which human arthritogenic and therapeutic anti-arthritic compositions are evaluated. Also provided herein are therapeutic oligopeptides derived from the variable regions of the TCRs of the transgenes of the invention and/or from the amino acid sequence of proteins comprising endogenous polypeptide arthritogenic antigens.

US PAT NO: 5,674,734 [IMAGE AVAILABLE] L24: 19 of 52
DATE ISSUED: Oct. 7, 1997
TITLE: Cell death protein
INVENTOR: Philip Leder, Chestnut Hill, MA
Brian Seed, Boston, MA
Ben Z. Stanger, Brookline, MA
Tae-Ho Lee, Daejeon, Republic of Korea
Emily Kim, Chestnut Hill, MA
ASSIGNEE: President and Fellows of Harvard College, Cambridge, MA (U.S. corp.)
The General Hospital Corporation, Boston, MA (U.S. corp.)
APPL-NO: 08/444,005
DATE FILED: May 18, 1995
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: Tekchand Saidha
LEGAL-REP: Clark & Elbing LLP

US PAT NO: 5,674,734 [IMAGE AVAILABLE] L24: 19 of 52

ABSTRACT:
Disclosed is a protein, designated RIP, which contains a death domain at its carboxy terminus and a kinase domain at its amino terminus. RIP interacts with the **Fas**/APO-1 intracellular domain and the TNFR1 intracellular domain. When expressed in transformed host cells, recombinant RIP promotes apoptosis. Also disclosed are DNA molecules encoding RIP, anti-RIP antibodies, and screening methods for discovering **inhibitors** of RIP-dependent apoptosis.

US PAT NO: 5,674,492 [IMAGE AVAILABLE] L24: 20 of 52
DATE ISSUED: Oct. 7, 1997
TITLE: Method of preventing or treating disease characterized by neoplastic cells expressing CD40
INVENTOR: Richard J. Armitage, Bainbridge Island, WA
William C. Fanslow, III, Federal Way, WA
Dan L. Longo, Kensington, MD
William J. Murphy, Frederick, MD
ASSIGNEE: Immunex Corporation, Seattle, WA (U.S. corp.)
The United States of America as represented by the Department of Health and Human Services, Washington, DC (U.S. govt.)
APPL-NO: 08/360,923
DATE FILED: Dec. 21, 1994
ART-UNIT: 186
PRIM-EXMR: Lila Feisee
ASST-EXMR: Phillip Gambel
LEGAL-REP: Patricia Anne Perkins

US PAT NO: 5,674,492 [IMAGE AVAILABLE] L24: 20 of 52

ABSTRACT:
There is disclosed a method of treating a mammal afflicted with a disease characterized by neoplastic cells that express CD40, comprising administering a therapeutically effective amount of a CD40 binding protein in a pharmaceutically acceptable buffer. CD40 binding proteins include **monoclonal** **antibodies** to CD40, and CD40 ligand. CD40 binding proteins may also be used to prevent disease characterized by neoplastic cells that express CD40, in individuals at risk for such disease.

US PAT NO: 5,672,603 [IMAGE AVAILABLE] L24: 21 of 52
DATE ISSUED: Sep. 30, 1997
TITLE: Apoptosis regulating composition
INVENTOR: Satoru Nakai, Tokushima-ken, Japan
Koutoku Aihara, Tokushima-ken, Japan
Hitomi Mori, Tokushima, Japan
Michiaki Tominaga, Tokushima-ken, Japan
Masakazu Adachi, Takasaki, Japan
Hiroyuki Ichikawa, Tokushima, Japan
Seiji Akamatsu, Naruto, Japan
Fumio Saito, Takasaki, Japan
ASSIGNEE: Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan (foreign corp.)
APPL-NO: 08/466,449
DATE FILED: Jun. 6, 1995
ART-UNIT: 125
PRIM-EXMR: Russell Travers
LEGAL-REP: Sughrue, Mion, Zinn, Macpeak & Seas

US PAT NO: 5,672,603 [IMAGE AVAILABLE] L24: 21 of 52

ABSTRACT:
An object of the invention is to provide an apoptosis regulating composition. According to the invention, an apoptosis regulating composition is provided which comprises, as an active ingredient at least one carbostyril derivatives of general formula (1) ##STR1## and salts thereof.

US PAT NO: 5,670,149 [IMAGE AVAILABLE] L24: 22 of 52
DATE ISSUED: Sep. 23, 1997
TITLE: Lymphotoxin-.beta., Lymphotoxin-.beta. complexes, pharmaceutical preparations and therapeutic uses thereof
INVENTOR: Jeffrey Browning, Brookline, MA
Carl F. Ware, Riverside, CA
ASSIGNEE: Biogen, Inc., Cambridge, MA (U.S. corp.)
The University of California, Oakland, CA (U.S. corp.)
APPL-NO: 08/476,489
DATE FILED: Jun. 6, 1995
ART-UNIT: 185
PRIM-EXMR: James Ketter
ASST-EXMR: Irem Yucel
LEGAL-REP: Kerry A. Flynn

US PAT NO: 5,670,149 [IMAGE AVAILABLE] L24: 22 of 52

ABSTRACT:
This invention relates to lymphotoxin-.beta., a lymphocyte membrane type protein. This protein is found on the surface of a number of cells, including phorbol ester (PNA) stimulated T cell hybridoma II-23.D7 cells. This invention also relates to complexes formed between lymphotoxin-.beta. and other peptides such as lymphotoxin-.alpha. and to complexes comprising multiple subunits of lymphotoxin-.beta.. These proteins and complexes are useful in holding LT-.alpha. formed within the cell on the cell surface where the LT-.alpha./LT-.beta. complex may act as an inflammation regulating agent, a tumor growth **inhibiting** agent, a T cell **inhibiting** agent, a T cell activating agent, an autoimmune disease regulating agent, or an HIV **inhibiting** agent. Furthermore, the antitumor activity of the LT-.alpha./LT-.beta. complex may be delivered to tumor cells by tumor infiltrating lymphocytes (TILs) transfected with the gene for LT-.beta..

US PAT NO: 5,665,874 [IMAGE AVAILABLE] L24: 23 of 52
DATE ISSUED: Sep. 9, 1997
TITLE: Cancer related antigen
INVENTOR: Francis P. Kuhajda, Lutherville, MD
Gary R. Pasternack, Baltimore, MD
ASSIGNEE: John Hopkins University, Baltimore, MD (U.S. corp.)
APPL-NO: 08/469,005
DATE FILED: Jun. 5, 1995
ART-UNIT: 189
PRIM-EXMR: George C. Elliott
ASST-EXMR: Jeffrey Fredman
LEGAL-REP: Baker & Botts, L.L.P.

US PAT NO: 5,665,874 [IMAGE AVAILABLE] L24: 23 of 52

ABSTRACT:
A method of determining the prognosis of a solid tumor is provided, in which a sample from a patient bearing a tumor is assayed for the presence of a protein which is immunologically cross-reactive with the hpr gene product, but not with haptoglobin 1 or haptoglobin 2. Also provided is a method for preparing antibodies specific for this diagnostic marker which correlates with early relapse and metastasis of breast and other cancers. The marker can be detected using immunological methods employing antibodies specific for Hpr protein and not cross-reactive with haptoglobins 1 or 2.

US PAT NO: 5,661,004 [IMAGE AVAILABLE] L24: 24 of 52
DATE ISSUED: Aug. 26, 1997
TITLE: Lymphotoxin-.beta., lymphotoxin-.beta. complexes, pharmaceutical preparations and therapeutic uses thereof
INVENTOR: Jeffrey Browning, Brookline, MA
Carl F. Ware, Riverside, CA
ASSIGNEE: Biogen, Inc., Cambridge, MA (U.S. corp.)
University of California, Oakland, CA (U.S. corp.)
APPL-NO: 08/484,272
DATE FILED: Jun. 7, 1995
ART-UNIT: 189
PRIM-EXMR: George C. Elliott
ASST-EXMR: Amy J. Nelson
LEGAL-REP: Kerry A. Flynn

US PAT NO: 5,661,004 [IMAGE AVAILABLE] L24: 24 of 52

ABSTRACT:
This invention relates to lymphotoxin-.beta., a lymphocyte membrane type protein. This protein is found on the surface of a number of cells,

including phorbol ester (PMA) stimulated T cell hybridoma II-23.D7 cells. This invention also relates to complexes formed between lymphotoxin-.beta. and other peptides such as lymphotoxin-.alpha. and to complexes comprising multiple subunits of lymphotoxin-.beta.. These proteins and complexes are useful in holding LT-.alpha. formed within the cell on the cell surface where the LT-.alpha./LT.beta. complex may act as an inflammation regulating agent, a tumor growth **inhibiting** agent, a T cell **inhibiting** agent, a T cell activating agent, an autoimmune disease regulating agent, or an HIV **inhibiting** agent. Furthermore, the antitumor activity of the LT-.alpha./LT-.beta. complex may be delivered to tumor cells by tumor infiltrating lymphocytes (TILs) transfected with the gene for LT-.beta..

US PAT NO: 5,658,912 [IMAGE AVAILABLE] L24: 25 of 52
DATE ISSUED: Aug. 19, 1997
TITLE: Apoptosis regulating composition
INVENTOR: Satoru Nakai, Tokushima-ken, Japan
Koutoku Aihara, Tokushima-ken, Japan
Hitomi Mori, Tokushima, Japan
Michiaki Tominaga, Tokushima-ken, Japan
Masakazu Adachi, Takasaki, Japan
Hiroyuki Ichikawa, Tokushima, Japan
Seiji Akamatsu, Naruto, Japan
Fumio Saito, Takasaki, Japan
ASSIGNEE: Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan (foreign corp.)
APPL-NO: 08/469,922
DATE FILED: Jun. 6, 1995
ART-UNIT: 125
PRIM-EXMR: Russell Travers
LEGAL-REP: Sughrue, Mion, Zinn, Macpeak & Seas

US PAT NO: 5,658,912 [IMAGE AVAILABLE] L24: 25 of 52

ABSTRACT:
An object of the invention is to provide an apoptosis regulating composition. According to the invention, an apoptosis regulating composition is provided which comprises, as an active ingredient, at least one carbostyril derivatives of general formula (1) ##STR1## and salts thereof.

US PAT NO: 5,654,146 [IMAGE AVAILABLE] L24: 26 of 52
DATE ISSUED: Aug. 5, 1997
TITLE: Human ice homolog
INVENTOR: Scott Michael Braxton, San Mateo, CA
Angelo M. Delegeane, Hayward, CA
Dinh Diep, San Francisco, CA
ASSIGNEE: Incyte Pharmaceuticals, Inc., Palo Alto, CA (U.S. corp.)
APPL-NO: 08/443,865
DATE FILED: May 31, 1995
ART-UNIT: 189
PRIM-EXMR: George C. Elliott
ASST-EXMR: Amy J. Nelson
LEGAL-REP: Barbara J. Luther, Lucy J.Incyte Pharmaceuticals, Inc. Billings

US PAT NO: 5,654,146 [IMAGE AVAILABLE] L24: 26 of 52

ABSTRACT:
The present invention provides nucleotide and amino acid sequences that identify and encode a new human interleukin-1 converting enzyme homolog (ICEY). The present invention also provides for expression vectors for the production of purified ICEY, hybridization probes for the detection of ICEY-encoding nucleotide sequences, genetically engineered host cells for the expression of ICEY, diagnostic tests for ICEY or for polynucleotides encoding ICEY, and use of the protein to produce antibodies capable of binding specifically to the protein and use of the protein to screen for **inhibitors**.

US PAT NO: 5,648,238 [IMAGE AVAILABLE] L24: 27 of 52
DATE ISSUED: Jul. 15, 1997
TITLE: Human protein kinase C **inhibitor** homolog
INVENTOR: Janice Au-Young, Berkeley, CA
Phillip R. Hawkins, Mountain View, CA
Jennifer L. Hillman, San Jose, CA
ASSIGNEE: Incyte Pharmaceuticals, Inc., Palo Alto, CA (U.S. corp.)
APPL-NO: 08/666,798
DATE FILED: Jun. 18, 1996
ART-UNIT: 189
PRIM-EXMR: George C. Elliott
ASST-EXMR: Amy J. Nelson
LEGAL-REP: Lucy J.Incyte Pharmaceuticals, Inc. Billings

US PAT NO: 5,648,238 [IMAGE AVAILABLE] L24: 27 of 52

ABSTRACT:
The present invention provides a polynucleotide (ipkc) which identifies and encodes a novel human protein kinase C **inhibitor** homolog (IPKC). The invention provides for genetically engineered expression vectors and host cells comprising the nucleic acid sequence encoding IPKC.

US PAT NO: 5,637,465 [IMAGE AVAILABLE] L24: 28 of 52
DATE ISSUED: Jun. 10, 1997
TITLE: Method for the detection of a programmed or induced cell death of eukaryotic cells
INVENTOR: Bernhard Trauth, Mannheim, Federal Republic of Germany
ASSIGNEE: Boehringer Mannheim GmbH, Mannheim, Federal Republic of Germany (foreign corp.)
APPL-NO: 08/245,583
DATE FILED: May 18, 1994
ART-UNIT: 186
PRIM-EXMR: Toni R. Scheiner
ASST-EXMR: Yvonne Eyler
LEGAL-REP: Felfe & Lynch

US PAT NO: 5,637,465 [IMAGE AVAILABLE] L24: 28 of 52

ABSTRACT:
The invention concerns a method for the detection of a programmed or induced cell death of eukaryotic cells as well as a suitable test kit for this method of detection.

US PAT NO: 5,632,994 [IMAGE AVAILABLE] L24: 29 of 52
DATE ISSUED: May 27, 1997
TITLE: **Fas** associated proteins
INVENTOR: John C. Reed, Carlsbad, CA
Takaaki Sato, San Diego, CA
ASSIGNEE: La Jolla Cancer Research Foundation, La Jolla, CA (U.S. corp.)
APPL-NO: 08/410,804
DATE FILED: Mar. 27, 1995
ART-UNIT: 187
PRIM-EXMR: Stephanie W. Zitomer
ASST-EXMR: Dianne Rees
LEGAL-REP: Campbell and Flores

US PAT NO: 5,632,994 [IMAGE AVAILABLE] L24: 29 of 52

ABSTRACT:
The present invention provides mammalian protein tyrosine phosphatases, human PTP-BAS type 4, human PTP-BAS type 5a and mouse PTP-BAS type 5b, each of which is a **Fas**-associated protein (FAP), nucleic acid molecules encoding a PTP-BAS type 4 or a PTP-BAS type 5 and antibodies specific for a PTP-BAS type 4 or for a PTP-BAS type 5. The invention also provides methods for identifying FAP's, which can associate with **Fas** and can modulate apoptosis. The invention also provides screening assays for identifying an agent that can effectively alter the association of a FAP with **Fas** and, therefore, can increase or decrease the level of apoptosis in a cell. The invention further provides methods of modulating apoptosis in a cell by introducing into the cell a nucleic acid molecule encoding a PTP-BAS or fragment of a PTP-BAS or an antisense nucleotide sequence, which is complementary to a portion of a nucleic acid molecule encoding a PTP-BAS. The invention also provides a method of using a reagent that can specifically bind to a FAP to diagnose a pathology that is characterized by an increased or decreased level of apoptosis in a cell. The invention also provides methods of modulating apoptosis in a cell by contacting the cell with an agent that effectively alters the association of a FAP and **Fas** in a cell or alters the activity of a FAP in a cell.

US PAT NO: 5,629,204 [IMAGE AVAILABLE] L24: 30 of 52
DATE ISSUED: May 13, 1997
TITLE: Peptide related to human programmed cell death and DNA encoding it
INVENTOR: Tasuku Honjo, Kyoto, Japan
Yasumasa Ishida, Newton, MA
Takashi Shinohara, Kyoto, Japan
ASSIGNEE: Ono Pharmaceutical Co., Ltd., Osaka, Japan (foreign corp.)
Tasuku Honjo, Kyoto, Japan (foreign corp.)
APPL-NO: 08/396,650
DATE FILED: Mar. 1, 1995
ART-UNIT: 184
PRIM-EXMR: Robert A. Wax
ASST-EXMR: G. E. Bugaisky
LEGAL-REP: Sughrue, Mion, Zinn, Macpeak & Seas

US PAT NO: 5,629,204 [IMAGE AVAILABLE] L24: 30 of 52

ABSTRACT:
A membrane protein related to human programmed cell death (PD-1) and DNA encoding the said protein is provided. PD-1 protein may be useful for the treatment of various infections, immunological depression or acceleration, or tumors etc.

US PAT NO: 5,620,889 [IMAGE AVAILABLE] L24: 31 of 52
DATE ISSUED: Apr. 15, 1997
TITLE: Human anti-**Fas** IgG1 **monoclonal** **antibodies**
INVENTOR: David H. Lynch, Bainbridge Island, WA
Mark R. Alderson, Bainbridge Island, WA
ASSIGNEE: Immunex Corporation, Seattle, WA (U.S. corp.)
APPL-NO: 08/322,805
DATE FILED: Oct. 13, 1994
ART-UNIT: 186
PRIM-EXMR: Susan A. Loring

US PAT NO: 5,620,889 [IMAGE AVAILABLE] L24: 31 of 52

ABSTRACT:
The present invention provides a panel of **monoclonal** **antibodies** and binding proteins which specifically bind to human **Fas** antigen. Some of the antibodies and binding proteins are capable of stimulating T cell proliferation, **inhibiting** binding of anti-**Fas** CH-11 **monoclonal** **antibody** to cells expressing **Fas** antigen, blocking anti-**Fas** CH-11 **monoclonal** **antibody**-mediated lysis of cells, and blocking **Fas** ligand-mediated lysis of cells. The invention also provides for therapeutic compositions comprising the **monoclonal** **antibodies**.

US PAT NO: 5,599,665 [IMAGE AVAILABLE] L24: 32 of 52
DATE ISSUED: Feb. 4, 1997
TITLE: Pseudomonas aeruginosa nucleic acids encoding exoenzyme S activity and use thereof in detecting pseudomonas aeruginosa infection
INVENTOR: Joseph T. Barbieri, New Berlin, WI
Dara W. Frank, West Allis, WI
Scott M. Kulich, West Allis, WI
ASSIGNEE: MCW Research Foundation, Milwaukee, WI (U.S. corp.)
APPL-NO: 08/171,299
DATE FILED: Dec. 21, 1993
ART-UNIT: 187
PRIM-EXMR: Kenneth R. Horlick
LEGAL-REP: Quarles & Brady

US PAT NO: 5,599,665 [IMAGE AVAILABLE] L24: 32 of 52

ABSTRACT:
A genetic construct containing a coding region for exoenzyme S activity

from Pseudomonas aeruginosa is disclosed. A essentially pure protein preparation of the 49 kDa form of exoenzyme S is also disclosed. The protein product of the genetic construct may be used to modify the RAS protein function in mammalian carcinomas, used as a vaccine, or used to diagnose Pseudomonas aeruginosa infection.

US PAT NO: 5,591,587 [IMAGE AVAILABLE] L24: 33 of 52
DATE ISSUED: Jan. 7, 1997
TITLE: Polypeptide-induced monoclonal receptors to protein ligands
INVENTOR: Henry L. Niman, Pittsburgh, PA
ASSIGNEE: The Scripps Research Institute, La Jolla, CA (U.S. corp.)
APPL-NO: 08/294,879
DATE FILED: Aug. 23, 1994
ART-UNIT: 183
PRIM-EXMR: Christine M. Nucker
ASST-EXMR: Jeffrey Stucker
LEGAL-REP: Lyon & Lyon

US PAT NO: 5,591,587 [IMAGE AVAILABLE] L24: 33 of 52

ABSTRACT:
Monoclonal receptors raised to immunogenic polyeptides whose amino acid residue sequences correspond to sequences of oncoprotein ligands are disclosed, as are method for the production of those receptors and products and methods that utilize them. The monoclonal receptors bind both to the oncoprotein ligand to a portion of which the polypeptide corresponds in sequence, and to the immunogenic polypeptide to which the receptors were raised.

US PAT NO: 5,583,160 [IMAGE AVAILABLE] L24: 34 of 52
DATE ISSUED: Dec. 10, 1996
TITLE: Methylsphingosine used to treat apoptosis
INVENTOR: Yasuyuki Igarashi, Seattle, WA
Sen-Itiroh Hakomori, Seattle, WA
ASSIGNEE: The Biomembrane Institute, Seattle, WA (U.S. corp.)
APPL-NO: 08/357,306
DATE FILED: Dec. 14, 1994
ART-UNIT: 125
PRIM-EXMR: Theodore J. Criares
LEGAL-REP: Sughrue, Mion, Zinn, Macpeak & Seas

US PAT NO: 5,583,160 [IMAGE AVAILABLE] L24: 34 of 52

ABSTRACT:
N-methylated sphingosine used to induce apoptosis.

US PAT NO: 5,563,039 [IMAGE AVAILABLE] L24: 35 of 52
DATE ISSUED: Oct. 8, 1996
TITLE: TNF receptor-associated intracellular signaling proteins and methods of use
INVENTOR: David V. Goeddel, South San Francisco, CA
Hailing Hsu, South San Francisco, CA
ASSIGNEE: Tularik, Inc., So. San Francisco, CA (U.S. corp.)
APPL-NO: 08/414,625
DATE FILED: Mar. 31, 1995
ART-UNIT: 182
PRIM-EXMR: John Ulm
LEGAL-REP: Flehr, Hohbach, Test, Albritton & Herbert

US PAT NO: 5,563,039 [IMAGE AVAILABLE] L24: 35 of 52

ABSTRACT:
A novel family of intracellular signaling proteins, exemplified by a Tumor Necrosis Factor Receptor-1 Associated Death Domain protein (TRADD), share a common TRADD sequence and include transducers of signals that modulate cell growth, differentiation and apoptosis. As such, the TRADD proteins, TRADD-encoding nucleic acids, and natural TRADD intracellular binding targets provide both important targets and means for therapeutic intervention. In particular, the invention provides isolated TRADDs and TRADD fragments, nucleic acids encoding the subject TRADDs and TRADD fragments or capable of selectively hybridizing to such TRADD-encoding nucleic acids, vectors and cells comprising TRADD-encoding nucleic acids, and TRADD-specific binding reagents. These compositions find use in diagnostic and therapeutic methods for disease associated with undesirable cell growth, migration, differentiation and/or cytokine signal responsiveness and methods and compositions for identifying lead compounds and pharmacological agents.

US PAT NO: 5,543,412 [IMAGE AVAILABLE] L24: 36 of 52
DATE ISSUED: Aug. 6, 1996
TITLE: Hepatitis treatment with carbostyril compounds
INVENTOR: Satoru Nakai, Tokushima-ken, Japan
Koutoku Aihara, Tokushima-ken, Japan
Hitomi Mori, Tokushima, Japan
Michiaki Tominaga, Tokushima-ken, Japan
Masakazu Adachi, Takasaki, Japan
Hiroyuki Ichikawa, Tokushima, Japan
Seiji Akamatsu, Naruto, Japan
Fumio Saito, Takasaki, Japan
ASSIGNEE: Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan (foreign corp.)
APPL-NO: 08/469,893
DATE FILED: Jun. 6, 1995
ART-UNIT: 125
PRIM-EXMR: Russell Treavers
LEGAL-REP: Sughrue, Mion, Zinn, Macpeak & Seas

US PAT NO: 5,543,412 [IMAGE AVAILABLE] L24: 36 of 52

ABSTRACT:
An object of the invention is to provide hepatitis therapy. According to the invention, an apoptosis regulating composition is provided which comprises, as an active ingredient, at least one carbostyril derivatives of general formula (1) ##STR1## and salts thereof.

US PAT NO: 5,538,863 [IMAGE AVAILABLE] L24: 37 of 52
DATE ISSUED: Jul. 23, 1996
TITLE: Expression system comprising mutant yeast strain and expression vector encoding synthetic signal peptide
INVENTOR: Virginia L. Price, Seattle, WA
ASSIGNEE: Immunex Corporation, Seattle, WA (U.S. corp.)
APPL-NO: 08/086,335
DATE FILED: Jul. 1, 1993
ART-UNIT: 185
PRIM-EXMR: Mindy Fleisher
ASST-EXMR: Philip W. Carter
LEGAL-REP: Kathryn A. Anderson

US PAT NO: 5,538,863 [IMAGE AVAILABLE] L24: 37 of 52

ABSTRACT:
A novel strain of Saccharomyces cerevisiae is useful as a host cell in the production of recombinant proteins. The novel S. cerevisiae cells transformed with a recombinant expression vector encoding a desired heterologous protein, preferably fused to a suitable N-terminal signal peptide, are cultivated under conditions that promote expression of the protein. Also provided are signal peptides derived by replacing the native signal peptidase cleavage site of a type I interleukin-1 receptor signal peptide with the tripeptide AlaXAla, wherein X represents an amino acid selected from Leu, Phe, and Gln. An expression system comprises a yeast host cell (preferably the novel S. cerevisiae strain) transformed with an expression vector comprising a promoter functional in yeast cells operably linked to DNA encoding the novel signal peptide, which is fused to the N-terminus of DNA encoding a desired heterologous protein.

US PAT NO: 5,510,255 [IMAGE AVAILABLE] L24: 38 of 52
DATE ISSUED: Apr. 23, 1996
TITLE: Plant fatty acid synthases
INVENTOR: Vic C. Knauf, 1013 Hillview La., Winters, CA 95694
Gregory A. Thompson, 5127 Cowell Blvd., Davis, CA 95616
APPL-NO: 07/978,687
DATE FILED: Feb. 1, 1993
ART-UNIT: 183
PRIM-EXMR: Patricia R. Moody

US PAT NO: 5,510,255 [IMAGE AVAILABLE] L24: 38 of 52

ABSTRACT:
By this invention, compositions and methods of use related to .beta.-ketoacyl-ACP synthase, hereinafter also referred to as "synthase", are provided. Also of interest are methods and compositions of amino acid and nucleic acid sequences related to biologically active plant synthase(s).
In particular, synthase protein preparations which have relatively high turnover (specific activity) are of interest for use in a variety of applications, in vitro and in vivo. Especially, protein preparations having synthase I and/or synthase II activities are contemplated hereunder. Synthase activities are distinguished by the preferential activity towards longer and shorter acyl-ACPs. Protein preparations having preferential activity towards shorter chain length acyl-ACPs are synthase I-type. Synthases having preferential activity towards longer chain length acyl-ACPs are synthase II-type. Of special interest are synthases obtainable from Ricinus communis.

US PAT NO: 5,475,099 [IMAGE AVAILABLE] L24: 39 of 52
DATE ISSUED: Dec. 12, 1995
TITLE: Plant fatty acid synthases
INVENTOR: Vic C. Knauf, Winters, CA
Gregory A. Thompson, Davis, CA
ASSIGNEE: Calgene Inc., Davis, CA (U.S. corp.)
APPL-NO: 07/721,761
DATE FILED: Jun. 26, 1991
ART-UNIT: 183
PRIM-EXMR: Patricia R. Moody

US PAT NO: 5,475,099 [IMAGE AVAILABLE] L24: 39 of 52

ABSTRACT:
By this invention, compositions and methods of use related to .beta.-ketoacyl-ACP synthase, hereinafter also referred to as "synthase", are provided. Also of interest are methods and compositions of amino acid and nucleic acid sequences related to biologically active plant synthase(s).
In particular, synthase protein preparations which have relatively high turnover (specific activity) are of interest for use in a variety of applications, in vitro and in vivo. Especially, protein preparations having synthase I and/or synthase II activities are contemplated hereunder. Synthase activities are distinguished by the preferential activity towards longer and shorter acyl-ACPs. Protein preparations having preferential activity towards shorter chain length acyl-ACPs are synthase I-type. Synthases having preferential activity towards longer chain length acyl-ACPs are synthase II-type. Of special interest are synthases obtainable from Ricinus communis.

US PAT NO: 5,447,851 [IMAGE AVAILABLE] L24: 40 of 52
DATE ISSUED: Sep. 5, 1995
TITLE: DNA encoding a chimeric polypeptide comprising the extracellular domain of TNF receptor fused to IgG, vectors, and host cells
INVENTOR: Bruce A. Beutler, Dallas, TX
Karsten Peppel, Dallas, TX
David F. Crawford, Irving, TX
ASSIGNEE: Board of Regents, The University of Texas System, Austin, TX (U.S. corp.)
APPL-NO: 07/862,495
DATE FILED: Apr. 2, 1992
ART-UNIT: 182
PRIM-EXMR: Garnette D. Draper
ASST-EXMR: K. Cochrane Carlson
LEGAL-REP: Arnold, White & Durkee

US PAT NO: 5,447,851 [IMAGE AVAILABLE] L24: 40 of 52

ABSTRACT:
The invention relates generally to DNA sequences encoding chimeric

polypeptides comprising extracellular portions of cytokine receptor polypeptides attached to a sequence encoding portions of IgG polypeptides. The invention relates generally, as well, to DNA sequences encoding chimeric polypeptides comprising extracellular portions of cytokine receptor polypeptides attached through oligomers encoding specifically cleavable peptide linkers to a sequence encoding portions of IgG heavy chain polypeptides More specifically, the invention relates to a construction in which a cDNA sequence encoding the extracellular domain of the human 55 kD TNF receptor is attached through an oligomer encoding a thrombin-sensitive peptide linker to a sequence encoding the F.sub.c portion and hinge region of a mouse IgGl heavy chain. The invention relates as well to uses of the chimeric polypeptide, including: use as a reagent for the **antagonism** and assay of TNF and lymphotoxin from diverse species; use as a means of determining the mechanism by which TNF, or analogs thereof, interacts with the TNF receptor; use as an antitumor reagent, particularly against placental tumors; and, use as a reagent capable of controlling birth.

US PAT NO: 5,126,240 [IMAGE AVAILABLE] L24: 41 of 52
DATE ISSUED: Jun. 30, 1992
TITLE: Hybridomas and monoclonal paratopic molecules to apolipoprotein A-I
INVENTOR: Linda K. Curtiss, 8926 Flanders Dr., San Diego, CA 92126
APPL-NO: 06/913,061
DATE FILED: Sep. 29, 1986
ART-UNIT: 187
PRIM-EXMR: Christine Nucker
ASST-EXMR: Laurie A. Scheiner

US PAT NO: 5,126,240 [IMAGE AVAILABLE] L24: 41 of 52

ABSTRACT:
Hybridomas and their secreted paratopic molecules that immunoreact with apolipoprotein A-I are disclosed, as are assay methods for determining the presence and amount of apo A-I, and diagnostic systems useful in performing those determinations. Monoclonal paratopic molecules secreted by hybridomas having ATCC accession numbers HB 9200, HB 9201, HB 9202, HB 9203 and HB 9204 are utilized.

US PAT NO: 5,035,995 [IMAGE AVAILABLE] L24: 42 of 52
DATE ISSUED: Jul. 30, 1991
TITLE: Test method involving substance-conjugated complement component C1q
INVENTOR: Fumiaki Taguchi, 14-1, Yokodai 5-chome, Sagamihara-shi, Kanagawa-ken, Japan
Isamu Mitsui, Yokohama, Japan
Kinichi Hara, Yokohama, Japan
Masaro Hayashi, Yokohama, Japan
Kunio Ezawa, Tokyo, Japan
Kenichi Fukunaga, Machida, Japan
Jun Kuranari, Machida, Japan
ASSIGNEE: Calpis Food Industry Co., Ltd., Tokyo, Japan (foreign corp.)
Fumiaki Taguchi, Kanagawa, Japan (foreign indiv.)
APPL-NO: 07/355,196
DATE FILED: May 22, 1989
ART-UNIT: 182
PRIM-EXMR: Sam Rosen
LEGAL-REP: Darby & Darby

US PAT NO: 5,035,995 [IMAGE AVAILABLE] L24: 42 of 52

ABSTRACT:
A substance-conjugated complement component C1q is provided. A substance such as signal emitting substances or cell function regulating substances is conjugated via a sulfur atom to at least one site of the component. The site is not involved in binding immunoglobulins. A marker-labelled complement component C1q is used for measuring a complement-binding antibody, an antigen, a neutralizing antibody or a substance produced internally of and at the surface of a cell or a microorganism by measuring the marker.

US PAT NO: 5,019,384 [IMAGE AVAILABLE] L24: 43 of 52
DATE ISSUED: May 28, 1991
TITLE: Immunonodulating compositions and their use
INVENTOR: Malcolm L. Gefter, Weston, MA
Jean G. Guillet, Paris, France
ASSIGNEE: Massachusetts Institute of Technology, Cambridge, MA (U.S. corp.)
APPL-NO: 07/434,548
DATE FILED: Nov. 13, 1989
ART-UNIT: 189
PRIM-EXMR: John Doll
ASST-EXMR: Christina Chan
LEGAL-REP: Bertram I. Rowland

US PAT NO: 5,019,384 [IMAGE AVAILABLE] L24: 43 of 52

ABSTRACT:
Novel methods or compositions are provided for modulating the immune system, so as to be able to selectively stimulate or inactivate lymphocytes in relation to a particular transplantation antigen content. Particularly, mixtures may be employed associated with the more common transplanatation antigens of a host population. In this manner, a large number of people can be treated, for example, by immunization, stimulation of particular T-cells or B-cells in relation to a pathogenic invasion of other aberrant state, e.g. neoplasia, treatment of autoimmune diseases, and the like. Particularly, the compositions may involve an oligopeptide involving as a first region a consensus sequence and an epitope or the first region may be joined to a second region comprising an antibody target sequence which is capable of competing with an epitopic site of an antigen of interest.

US PAT NO: 5,015,571 [IMAGE AVAILABLE] L24: 44 of 52
DATE ISSUED: May 14, 1991
TITLE: Polypeptide-induced monoclonal receptors to protein ligands
INVENTOR: Henry L. Niman, Carlsbad, CA
Richard A. Lerner, La Jolla, CA
ASSIGNEE: Scripps Clinic and Research Foundation, La Jolla, CA (U.S. corp.)
APPL-NO: 07/039,534
DATE FILED: Apr. 16, 1987
ART-UNIT: 187
PRIM-EXMR: Robert A. Wax
ASST-EXMR: J. Stucker
LEGAL-REP: Lyon & Lyon

US PAT NO: 5,015,571 [IMAGE AVAILABLE] L24: 44 of 52

ABSTRACT:
Monoclonal receptors raised to immunogenic polypeptides whose amino acid residue sequences correspond to sequences of oncoprotein ligands are disclosed, as are method for the production of those receptors and products and methods that utilize them. The monoclonal receptors bind both to the oncoprotein ligand to a portion of which the polypeptide corresponds in sequence, and to the immunogenic polypeptide to which the receptors were raised.

US PAT NO: 4,960,702 [IMAGE AVAILABLE] L24: 45 of 52
DATE ISSUED: Oct. 2, 1990
TITLE: Methods for recovery of tissue plasminogen activator
INVENTOR: Craig Rice, Alameda, CA
Michael J. Morser, San Francisco, CA
Charles Glaser, San Francisco, CA
Peter A. Donner, Berlin, Federal Republic of Germany
ASSIGNEE: Codon, South San Francisco, CA (U.S. corp.)
APPL-NO: 07/167,061
DATE FILED: Mar. 11, 1988
ART-UNIT: 188
PRIM-EXMR: Elizabeth C. Weimar
ASST-EXMR: Charles L. Patterson
LEGAL-REP: Townsend and Townsend

US PAT NO: 4,960,702 [IMAGE AVAILABLE] L24: 45 of 52

ABSTRACT:
Methods for recovering t-PA from a liquid medium are disclosed. The methods comprise contacting a liquid medium with at least one substrate capable of effecting a separation of intact t-PA from degraded t-PA thereafter recovering the intact t-PA free from other unrelated protein. The present invention also provides compounds produced by this method, compounds comprising intact one-chain t-PA and pharmaceutical compositions containing them and methods for using such compositions.

US PAT NO: 4,882,423 [IMAGE AVAILABLE] L24: 46 of 52
DATE ISSUED: Nov. 21, 1989
TITLE: Substance-conjugated complement component C1q
INVENTOR: Fumiaki Taguchi, 14-1, Yokodai 5-chome, Sagamihara-shi, Kanagawa-ken, Japan
Isamu Mitsui, Yokohama, Japan
Kinichi Hara, Yokohama, Japan
Masaro Hayashi, Yokohama, Japan
Kunio Ezawa, Tokyo, Japan
Kenichi Fukunaga, Tokyo, Japan
Jun Kuranari, Tokyo, Japan
ASSIGNEE: Calpis Food Industry, both of, Japan (foreign corp.)
Fumiaki Taguchi, both of, Japan (foreign indiv.)
APPL-NO: 07/032,025
DATE FILED: Mar. 30, 1987
ART-UNIT: 182
PRIM-EXMR: Sam Rosen
LEGAL-REP: Darby & Darby

US PAT NO: 4,882,423 [IMAGE AVAILABLE] L24: 46 of 52

ABSTRACT:
A substance-conjugated complement component C1q is provided. A substance such as signal emitting substances or cell function regulating substances is conjugated via a sulfur atom to at least one site of the component. The site is not involved in binding immunoglobulins. A marker-labelled complement component C1q is used for measuring a complement-binding antibody, an antigen, a neutralizing antibody or a substance produced internally of and at the surface of a cell or a microorganism by measuring the marker.

US PAT NO: 4,828,986 [IMAGE AVAILABLE] L24: 47 of 52
DATE ISSUED: May 9, 1989
TITLE: Assay method and diagnostic system for determining the ratio of APO B-100 to APO A-I in a blood sample
INVENTOR: Richard S. Smith, Del Mar, CA
Doreen M. Hogle, San Diego, CA
Linda K. Curtiss, San Diego, CA
Joseph L. Witztum, San Diego, CA
Steven Young, San Diego, CA
ASSIGNEE: Scripps Clinic and Research Foundation, La Jolla, CA (U.S. corp.)
APPL-NO: 06/913,140
DATE FILED: Sep. 29, 1986
ART-UNIT: 182
PRIM-EXMR: Robert J. Warden
ASST-EXMR: Stephen C. Wieder
LEGAL-REP: Dressler, Goldsmith, Shore, Sutker & Milnamow, Ltd.

US PAT NO: 4,828,986 [IMAGE AVAILABLE] L24: 47 of 52

ABSTRACT:
Methods of determining the ratio of apolipoprotein B-100 to apolipoprotein A-I using ELISA techniques in conjunction with monoclonal paratopic molecules are disclosed as are diagnostic systems useful in performing those determinations. Monoclonal paratopic molecules secreted by hybridomas having ATCC accession numbers HB 8742, HB 8746, HB 9200 and HB 9201 are utilized.

US PAT NO: 4,529,693 [IMAGE AVAILABLE] L24: 48 of 52
DATE ISSUED: Jul. 16, 1985
TITLE: Detecting neoplastic mammary epithelial cells by detecting

thioesterase II marker
INVENTOR: Stuart Smith, Lafayette, CA
Louis J. Libertini, Corvallis, OR
Betty J. Thompson, San Francisco, CA
ASSIGNEE: Children's Hospital Medical Center of Northern California, Oakland, CA (U.S. corp.)
APPL-NO: 06/560,030
DATE FILED: Dec. 9, 1983
ART-UNIT: 128
PRIM-EXMR: Sidney Marantz
LEGAL-REP: Townsend and Townsend

US PAT NO: 4,529,693 [IMAGE AVAILABLE] L24: 48 of 52

ABSTRACT:
Methods are provided for detecting thioesterase II enzyme in both tissue and serum samples. The presence of thioesterase II in other than mammary epithelial tissue is associated with neoplastic mammary epithelial cells.

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[redacted]000709097A1 L24: 51 of 52

ABSTRACT:

The present invention relates to a therapeutic agent for rheumatic disease comprising an anti-**Fas** **monoclonal** **antibody**, or the combination of an anti-**Fas** **monoclonal** **antibody** and a medical substance having an **inhibitory** effect of cell proliferation as an active ingredient. The anti-**Fas** **monoclonal** **antibody** of this invention reacts with the **Fas** antigen in synovial cells of patients with rheumatoid arthritis, especially the human **Fas** antigen specifically and expresses apoptosis on synovial cells. <IMAGE>

WO009510540A1 L24: 52 of 52

ABSTRACT:

<CHG DATE=19950607 STATUS=O>The present invention provides a panel of **monoclonal** **antibodies** and binding proteins which specifically bind to human **Fas** antigen. Some of the antibodies and binding proteins are capable of stimulating T cell proliferation, **inhibiting** binding of anti-**Fas** CH-11 **monoclonal** **antibody** to cells expressing **Fas** antigen, blocking anti-**Fas** CH-11 **monoclonal** **antibody**-mediated lysis of cells, and blocking **Fas** [redacted]gand-mediated lysis of cells. The invention also provides for [redacted]erapeutic compositions comprising the **monoclonal** **antibodies**.

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FILE 'USPAT, JPO, EPO' ENTERED AT 14:33:15 ON 07 MAY 1998
FILE 'USPAT'
L1 511 S FAS
FILE 'JPO'
L2 95 S FAS
FILE 'EPO'
L3 32 S FAS
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L4 638 S FAS
FILE 'USPAT'
L5 1400039 S INHIB? OR REDUC? OR SUPPRESS? OR ANTAGON?
FILE 'JPO'
L6 803500 S INHIB? OR REDUC? OR SUPPRESS? OR ANTAGON?
FILE 'EPO'
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FILE 'JPO'
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FILE 'EPO'
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